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PREVALENCE OF RICKETS IN CHILDREN BETWEEN TWO AND FOURTEEN YEARS OF AGE

CAPTAIN RICHARD H. FOLLIS JR.
ARMY OF THE UNITED STATES

DEBORAH JACKSON, B.S.
BALTIMORE

MARTHA M. ELIOT, M.D.
WASHINGTON, D. C.
AND
E. A. PARK, M.D.
BALTIMORE

Rickets can be recognized at autopsy with great accuracy at its very beginning by means of histologic examination of the skeleton. All clinical methods for determining rickets are inaccurate and much inferior by comparison. The classic study by Schmorl [1] of the prevalence of rickets in Dresden, Germany, between the years 1901 and 1908 was based on the examination in consecutive autopsies of 386 children aged between 2 months and 5 years. Schmorl reported that in the third month of life the prevalence was 61 per cent, from the fourth to the eighteenth month 94 to 98 per cent, from the nineteenth month to the beginning of the third year 91 per cent, in the third year 88 per cent and in the fourth year 71 per cent. He did not determine the prevalance after the fourth year, because of the conviction that the disease occurred infrequently after that age. He wrote: "Since 1906 I have limited my study to the first four years of life, after I recognized that the number of cases discovered after that age was not proportional to the toil involved in the examination for the disease, even though in the later years of childhood now and then a case of late rickets may be brought to light." At first thought it seems peculiar that Schmorl should have considered rickets after the fourth year exceptional when he had reported it in 71 per cent of the children dying during the fourth year. This is the explanation: He divided his cases into instances of "beginning," "florid," "healing" and "healed" rickets. By "healed" rickets he meant that the disease had ceased and only scars and deformities remained. In the fourth year the rickets was "healed" in 56 per cent (14 cases) and active in only 14.7 per cent (5 cases, 2 of "florid" and 3 of "healing" rickets).

The presidential address (unpublished) delivered by Dr. E. A. Park at the meeting of the American Pediatric Society, at Skytop, Pa., April 30, 1942, was based on the data contained in this report.

From the Departments of Pediatrics and Pathology, Johns Hopkins University School of Medicine and the Harriet Lane Home of the Johns Hopkins Hospital, and the Children's Bureau, United States Department of Labor.

1. Schmorl, G.: Die pathologische Anatomie der rachitischen Knochenerkrankung mit besonderer Berücksichtigung ihrer Histologie und Pathogenese, Ergeb. d. inn. Med. u. Kinderh. **4**:403, 1909.

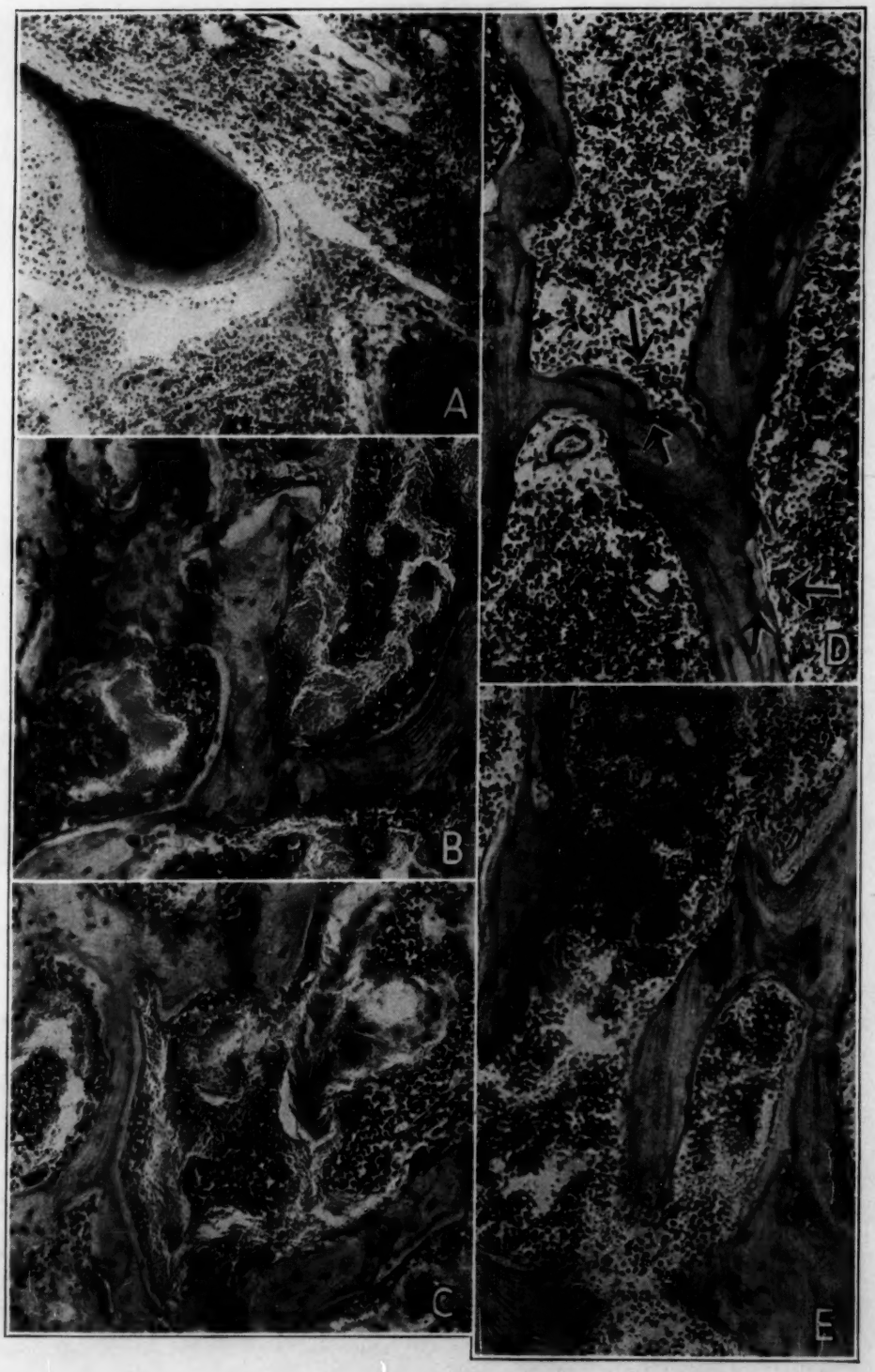

Figure 1

(See legend on opposite page)

This explanation of Schmorl's figures is important in the light of ours, because in our study we have made no attempt whatsoever to record rickets no longer active.

Since its publication, in 1909, Schmorl's work has remained the only authentic study on the age prevalence of rickets and has been largely responsible for the belief in the almost universal occurrence of the disease during the first two years of life. Schmorl's opinion, just quoted, has lent support to the impression that rickets is extremely rare in the later years of childhood. With the exception of that part of Schmorl's studies which covered the third and fourth years of life we know of no studies of any kind concerning the prevalence of rickets after the second year of life.

Our study on the prevalence of rickets in older children is part of a larger study of the prevalence from birth to 14 years which was begun in 1927 and has been continued to the present. Consecutive postmortem examinations have been made on 1,475 children. Of these, 260 were between 2 and 14 years of age. This report is concerned with the prevalence of rickets in these 260 children.

METHODS

The bones studied were the middle ribs. These were with few exceptions the only bones available. Fortunately, it so happens that ribs are the most favorable bones for the early detection of rickets, inasmuch as the disease becomes recognizable earlier and advances more rapidly at the anterior costochondral junctions than in any other bone.

The method of decalcification used from 1927 to 1934 was the formic acid method as described by Schmorl.[2] The bones were sawed into slabs 3 to 5 mm. in thickness and were placed for three days in a solution composed of equal parts of "technical" formic acid and solution of formaldehyde U. S. P. diluted to 10. They were then placed in changes of 80 per cent alcohol to which had been added an excess of tribasic magnesium phosphate ($Mg_3[PO_4]_2.7H_2O$). After neutralization of the acid the slabs were washed for twenty-four hours in running water.

Beginning with 1934 decalcification was performed according to the nitric acid method employed by Stacy Guild and associates.[3] The slabs were placed in changes of a 1 per cent solution of nitric acid in solution of formaldehyde U. S. P. diluted 1 to 10. The end point

2. Schmorl, G.: Die pathologisch histologischen Untersuchungsmethoden, Berlin, F. C. W. Vogel, 1934.

3. Crowe, S. J.; Guild, S. R., and Polvogt, L. M.: Observations on the Pathology of High-Tone Deafness, Bull. Johns Hopkins Hosp. **54**:315, 1934.

EXPLANATION OF FIGURE 1

A, photomicrograph of bone from J. J., a Negro boy 1 year 7 months old. The cause of death was subarachnoid hemorrhage, acute nutritional disturbance and dehydration. The rickets was advanced. The photomicrograph is inserted merely to illustrate the osteoid borders in a histologic preparation made according to the McLean-Bloom technic. The bone was hardened in solution of formaldehyde and cut without decalcification and stained with silver nitrate. The osteoid border in normal bones, the "physiologic osteoid," was visible with the same clearness in preparations made according to the McLean-Bloom technic as in our decalcified preparations stained with hematoxylin and eosin. *B*, photomicrograph of bone from A. C., a white girl 8½ years old. The final diagnosis was septicemia caused by Haemophilus influenzae; the illness lasted two days. The osteoid borders were interpreted to mean moderate rickets. No signs of rickets were found at the cartilage-shaft junction. *C*, photomicrograph of bone from J. B., a Negro girl 12½ years old. The final diagnosis was meningococcic meningitis. The duration of illness was five days. The osteoid indicated moderate rickets. The region of the costochondral junction had a normal appearance. *D*, photomicrograph of bone from R. T., a Negro boy 10 years old. The diagnosis was rheumatic heart disease with heart failure. The duration of illness was more than five months. The osteoid in the histologic section indicated slight rickets. *E*, photomicrograph of bone from I. Y., a white girl of 5 years. Her associated illness was pertussis for two weeks and pertussis encephalitis for three days. Histologic examination indicated moderate rickets.

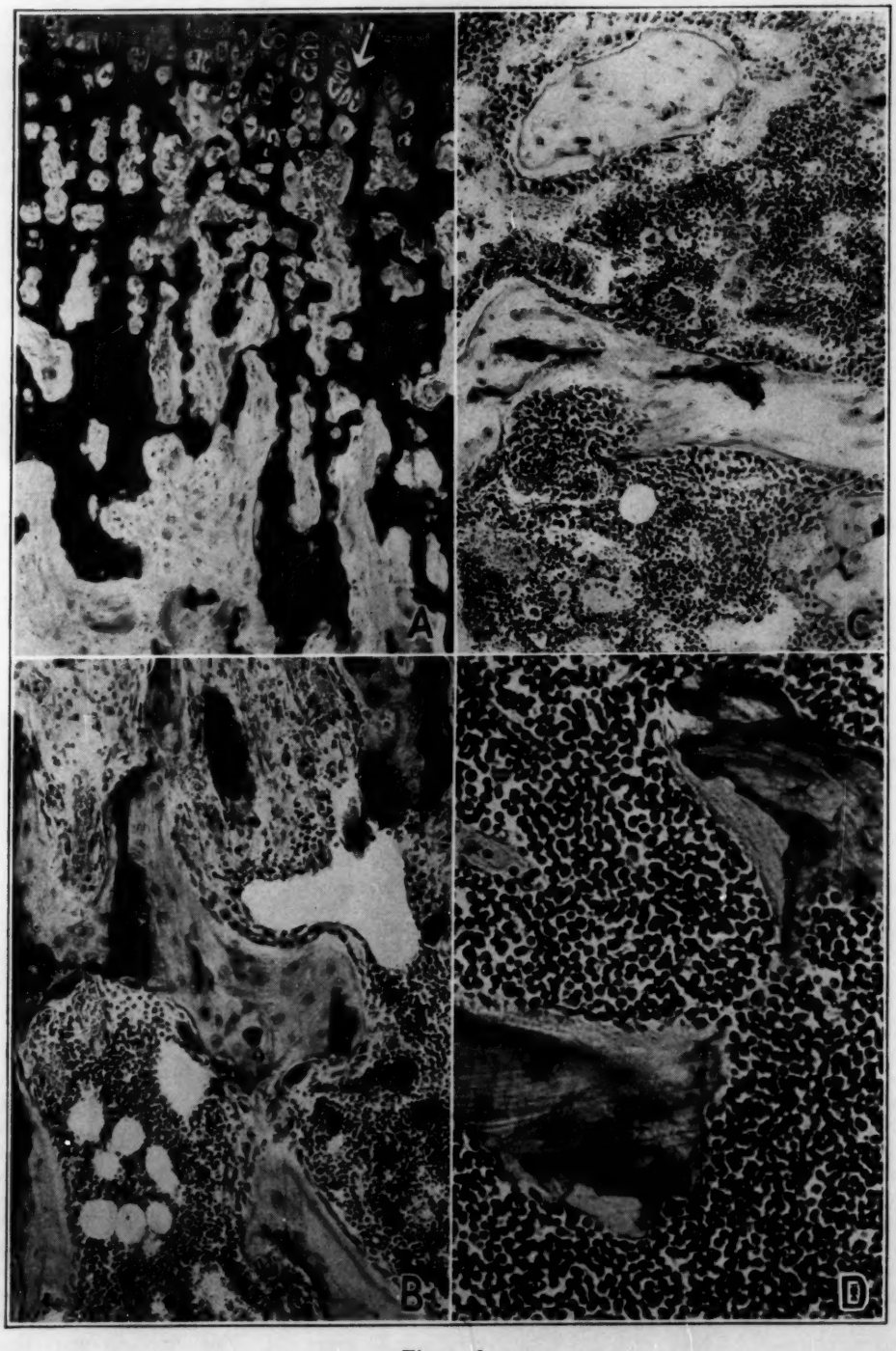

Figure 2

(See legend on opposite page)

was tested daily by addition of a small sample from the bottom of the jar to a solution composed of one part of 5 per cent ammonium carbonate ($[NH_4]_2C_2O_4$) and two parts of 5 per cent ammonium hydroxide (NH_4OH). Decalcification was regarded as satisfactory when the test fluid remained clear of any precipitate. The bones were left in the decalcifying fluid for twenty-four hours after this negative result had been obtained. Deacidification was obtained by placing the slabs in 5 per cent solution of sodium sulfate (Na_2SO_4) for forty-eight hours or longer with one change followed by washing in running tap water for twenty-four hours.

A celloidin (pyroxylin) technic was employed. Bones decalcified according to the formic acid method were cut in sections 20 microns thick, and those decalcified in nitric acid, in sections 14 microns thick. The stains routinely employed were hematoxylin and eosin.

On account of the statement of McLean and Bloom [4] that decalcification gives rise to false appearances of osteoid borders and defects in calcification of the cartilage, we made additional preparations in 12 cases from undecalcified material according to the technic recommended by them. These were stained with silver nitrate. On comparison of the preparations made according to the McLean-Bloom technic we came to the conclusion that our preparations were valid and gave reliable pictures of the state of calcification. The osteoid borders were just as plain in the undecalcified preparations stained with silver nitrate ($AgNo_3$) as in the decalcified preparations stained with hematoxylin and eosin; the deposits of calcium and phosphate in the cartilage were more conspicuous and more easily recognized in the undecalcified sections stained with silver nitrate, but they were visible in the decalcified preparations stained with hematoxylin and eosin.

Roentgenograms of all bones were regularly taken after removal at autopsy, but they did not prove of importance in establishing the disease.

Our criteria of rickets were the familiar appearances at the cartilage-shaft junctions, consisting in defects of calcification, irregularities in invasion of the cartilage, etc., and osteoid borders of abnormal thickness in the shaft. Breadths of osteoid in excess of those usually seen on the trabeculae of the ribs of normal premature infants were considered abnormal and indicative of rickets. The proviso was made, however, that such osteoid borders be on the trabeculae in the interior of the shaft and not in the cortex, for in healthy children growing rapidly wide borders of osteoid are often found along the cortex. In infants the characteristic changes at the cartilage-shaft junctions and the abnormally wide osteoid borders are almost always found together, and the two were commonly found together in the younger age groups. In the older children, in whom the rate of growth of the cartilage had become considerably reduced, it was common to find the changes limited to the osteoid borders. The microscopic picture in the older children was then similar to that found in adults with osteomalacia, in whom the evidence of the disease of necessity is limited to abnormal breadth of osteoid (figs. 1 and 2).

We classified the rickets as slight, moderate and advanced. By slight we meant slight defects in calcification at the cartilage-shaft junction and invasion of the cartilage by the blood vessels for only very short distances or osteoid borders slightly but definitely exceeding those normal for the rapidly growing premature infant. We termed the condition advanced rickets either when the osteoid borders were several times the width found in the healthy premature infant or when the defective calcification at the cartilage-shaft junction was very marked, the invasion of the cartilage had assumed mass proportions and the vessels

4. McLean, F. C., and Bloom, W.: Calcification and Ossification: Calcification in Normal Growing Bone, Anat. Rec. **78**:333, 1940.

EXPLANATION OF FIGURE 2

A, photomicrograph of bone from L. R., a Negro girl 3 years old. The final diagnosis was lead poisoning with lead encephalopathy. The encephalopathic symptoms were of a few days' duration, but the symptoms of lead poisoning were at least of one month's duration. The rachitic changes at the cartilage-shaft junction were slight but definite. They appeared in the background of the classic histologic picture of lead osteochondropathy. *B*, photomicrograph of a section from the shaft of the rib shown in *A*. The excessive osteoid production indicated moderate rickets. *C*, photomicrograph of bone from R. M., a 5 year old Negro boy. Death occurred after an unexplained illness of two days' duration. The osteoid borders indicated moderate rickets. *D*, photomicrograph of bone from W. W., a white boy 4½ years old. The final diagnosis was acute lymphoid leukemia. The duration of illness was four months. The osteoid in histologic sections indicated advanced rickets.

extended far into the accumulated proliferative cartilage. We classified the condition moderate when the changes were intermediate. As previously stated, we did not include healed rickets.

When characteristic changes were found at the cartilage-shaft junction, the classification was easy; the great difficulty was encountered in those cases in which the changes were limited to abnormally wide osteoid borders. Our division into slight, moderate and advanced rickets was arbitrary and undoubtedly inaccurate, but, on the other hand, we did not consider errors in degree of much importance. It should also be pointed out that in our final analysis we examined all the cases of each age group together. Hence our decisions as to classification were based on careful comparisons with children of corresponding age as well as on the general features of the disease.

TABLE 1.—*Prevalence of Rickets According to Age and Color*

	Age Prevalence				Color Prevalence					
					White			Negro		
Age, Years	No. of Subjects	With Rickets	Without Rickets	Percentage with Rickets	No. of Subjects	With Rickets	Percentage	No. of Subjects	With Rickets	Percentage
2- 3.....	67	38	29	57	22	13	60	45	25	55
3- 4.....	36	18	18	50	18	9	50	18	9	50
4- 5.....	29	11	18	38	10	2	20	19	10	53
5- 6.....	19	8	11	42	5	2	40	14	6	43
6- 7.....	15	5	10	33	6	1	16	9	4	44
7- 8.....	14	6	8	43	8	6	70	6	0	0
8- 9.....	15	7	8	47	6	4	66	9	3	33
9-10.....	9	2	7	22	6	0	0	3	2	66
10-11.....	8	5	3	62	3	1	33	5	4	80
11-12.....	9	4	5	44	6	3	50	3	1	33
12-13.....	5	2	3	40	3	1	33	2	1	50
13-14.....	4	1	3	25	2	0	0	2	1	50
	230	107	123	46.5	94	41	43.6	136	66	48.5

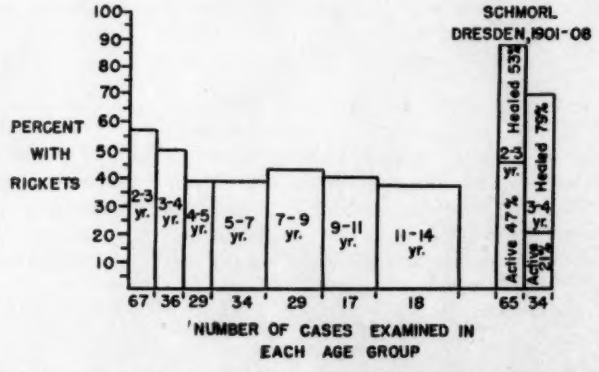

Fig. 3.—Graphic representation of the prevalence of rickets in the various age groups studied. Schmorl's results for the third and fourth years of life are added for comparison.

RESULTS

Total Prevalence.—Of the 230 children between 2 and 14 years, 107, or 46.5 per cent, were found to have rickets (table 1 and fig. 3). In table 1 are given figures for the prevalence for each year of age. In figure 3 the prevalence is shown in graphic form. Since the number of patients in the later age groups is small, the data for the 5 and 6, 7 and 8, 9 and 10, and 11, 12 and 13 year groups have been joined. Schmorl's figures for the prevalence of rickets, with the cases of "healed" rickets indicated, in the third and fourth years of life have been added for the purposes of comparison.

As seen from our data, the incidence is highest during the third year of life. From the fourth to the fourteenth birthday it remains at about 40 per cent. The total prevalence of active rickets found by Schmorl for the third year of life was 47 per cent and for the fourth year only 21 per cent.

In 23 per cent (53 cases) the disease was classified as slight, in 18.7 per cent (43 cases) moderate and in 4.8 per cent (11 cases) advanced.

Prevalence and Severity According to Color.—In table 1 is shown the prevalence according to color in each age group. Among the white children the total prevalence was 43.6 per cent, while among the Negro children it was 48.5 per cent. This finding is contrary to the belief that rickets is more frequent in Negroes. However, as will be seen in table 2, the total prevalence of moderate and advanced rickets was 27 per cent in Negroes as compared with 18 per cent in white subjects, and all the instances of advanced rickets occurred in Negroes. Thus, well developed rickets was definitely commoner in Negro children.

TABLE 2.—*Degree of Rickets in Relation to Total Number of Subjects of Each Color*

	White		Negro	
Degree	Number of Subjects	Percentage	Number of Subjects	Percentage
Slight	24	25.5	29	21.3
Moderate	17	18.1	26	19.1
Advanced	0	0	11	8.1
Total number of subjects examined	94	43.6	136	48.5

TABLE 3.—*Relation of Duration of Associated Disease to Prevalence and Severity of Rickets*

	Duration of Associated Disease		
	Acute (1-14 Days)	Intermediate (15-28 Days)	Chronic (29 Days or More)
Total number of subjects	79	37	114
Number and percentage with rickets	53 or 67%	7 or 21%	47 or 41%
Number and percentage of slight degree	26 or 49%	7 or 21%	20 or 42.5%
Number and percentage of moderate degree	23 or 43%	0	20 or 42.5%
Number and percentage of advanced degree	4 or 7.5%	0	7 or 15%

Acute illness was arbitrarily selected as lasting from one to fourteen days; chronic, more than twenty-nine days.

Prevalence and Severity of the Rickets in Relation to Duration of the Final Illness.—For purposes of analysis, final illnesses lasting fourteen days or less were classed as acute, those between fifteen and twenty-eight days as intermediate and those lasting more than twenty-eight days as chronic. The data bearing on the relation of the duration of the illness to the rickets will be found in table 3. Of all the children dying of acute illness, those showing rickets comprised 67 per cent (53 children), as compared with 41 per cent (47 children) for the group dying from chronic illness. This difference is statistically significant. When the duration of the disease was considered in relation to the severity of the rickets, not much difference was found. Forty-nine per cent (26 children) in the group with acute illness showed slight rickets, as compared with 43 per cent (20 children), in the group with chronic illness. Four, or 7.5 per cent, of the children showing advanced rickets fell into the group with acute illness, and 7, or 15 per cent, into the group with chronic illness.

Association with Particular Diseases.—Of 13 children dying of leukemia (fig. 2*D*) 6, or 46 per cent, had rickets. Two were Negro, and 4 were white. Three of the 6 received vitamin D, and 1, in spite of more than adequate vitamin D therapy, showed advanced changes in the bones. This patient's case in particular brought up the question whether leukemia could have any influence per se on the development of rickets. Roentgenographic studies of the skeletons of persons with leukemia usually reveal rarefaction, often extreme. The possibility that calcium salts become inadequate for ossification in the presence of leukemia must be considered. Lawrence and collaborators [5] have found that leukemic mice do not react normally to the administration of radioactive phosphorus. Tissue infiltrated with leukemic cells took up the element in larger quantities than normal lymph nodes; this apparently occurred at the expense of the bone. In other words, the lymphoid elements seemed to "steal" the available phosphorus from the bone. In our cases we have no evidence of this, but from the experiments cited such a relationship is an interesting speculation. Our data are too few to have statistical importance.

Forty-six children died of tuberculosis. Of these, 14, or 30 per cent, had rickets. All but 1 of these 14 children were Negroes, and the 5 showing advanced rickets were all Negroes. Obviously, racial and perhaps economic factors are involved.

TABLE 4.—*Seasonal Prevalence of Rickets*

Season	Total Number of Subjects	With Rickets	Percentage
Winter (December to February)	45	28	62
Spring (March to May)	73	31	42.5
Summer (June to August)	58	26	45
Autumn (September to November)	52	20	38.4

There were 14 instances of lead poisoning (fig. 2*A* and *B*). Of 9 children in whom the poisoning was acute, 3, or 33 per cent, had rickets; of the 5 who suffered from chronic lead poisoning all had rickets. This high incidence in children with chronic lead poisoning is probably significant and perhaps may be explained by the formation of insoluble lead phosphate compounds in the intestine and the consequent failure of absorption of phosphorus.

Of the 30 children having rheumatic fever, half had rickets. Three were white, and 12 were Negro. Again the results are not of significance.

The other causes of death varied and bore no specific relationship to the prevalence of rickets.

Influence of Season.—In table 4 will be found our data bearing on the seasonal incidence of rickets. The highest prevalence of rickets in our series occurred during the winter months, December to February, while in the autumn months, September to November, it reached its lowest point. This is in accord with the general belief in regard to the seasonal incidence of the disease.

5. Lawrence, J. H., and Scott, K. G.: Comparative Metabolism of Phosphorus in Normal and Lymphomatous Animals, Proc. Soc. Exper. Biol. & Med. **40**:694, 1939. Lawrence, J. H.; Tuttle, L. W.; Scott, K. G., and Connor, C. L.: Studies on Neoplasms with the Aid of Radioactive Phosphorus: I. The Total Phosphorus Metabolism of Normal and Leukemic Mice, J. Clin. Investigation **19**:267, 1940. Erf, L. A., and Lawrence, J. H.: Clinical Studies with the Aid of Radioactive Phosphorus: I. The Absorption and Distribution of Radiophosphorus in the Blood and Its Excretion by Normal Individuals and Patients with Leukemia, ibid. **20**:567, 1941.

COMMENT

Rickets was evident in the roentgenograms taken at autopsy of only 3 of the 38 children between 2 and 3 years, of only 2 of the 18 children between 3 and 4 years and of only 1 child of the 11 between 4 and 5 years. In none of the children between the ages of 5 and 14 years were there any signs of rickets in the postmortem roentgenogram. This failure of roentgen examination to reveal the rickets is not in the least remarkable, because the changes in the bones which give rise to the characteristic appearance of rickets in the roentgenogram, except when the rickets is extremely advanced, are those at the cartilage-shaft junction, and the changes at the cartilage-shaft junction in our cases were not sufficiently developed to show in the film because of the slowness with which growth in length was proceeding except in 1 or 2 of the younger children. Too few clinical roentgenograms were taken to be of any value in analysis.

We were totally unable to use Schmorl's [1] classification of "beginning," "florid," "healing" and "healed" rickets and do not believe that it is sound. In the first place, we could not differentiate regularly between "beginning" rickets and slight rickets which had been present for a long time but had remained in a state of only slight development. Moreover, we could not distinguish in many instances between "healing" rickets and a very common chronic form of the disease in which a healing process is operative all the time but never becomes sufficient to end the disease. We made no attempt to note those cases in which the rickets had entirely healed and only deformities were left.

The physical examinations were made by different physicians, many of them interns, and the recorded data in the clinical charts bearing on the presence or absence of the disease are not accurate enough for analysis. The true recognition of rickets from enlargements of the ends of the long bones is exceedingly difficult. The roentgenogram is a far more delicate means of determining rickets than physical examination. Since rickets could be recognized in the postmortem roentgenograms of but 6 of the 107 children showing the disease, it is safe to conclude that a clinical diagnosis was not possible except at most in a very few instances.

It is interesting that the prevalence of rickets among the children dying of acute disease was so much higher (67 per cent) than among those dying from chronic disease (41 per cent) or among those in the intermediate group (21 per cent). We are unable to explain the difference. Theoretically, and as borne out by our own experience, illness may either favor or interfere with the development of rickets. For example, infantile tetany, a syndrome which occurs in rickets when the serum calcium level is low, serves as an indicator of the underlying rickets. It is a common experience to find that latent tetany becomes manifest while infection is present and that the tetany remains resistant to treatment while the infection persists. Moreover, we have encountered instances in our pathologic studies of the skeleton in which vitamin D had failed to exert its expected curative action in the presence of illness. Illness can favor the development of rickets in other ways than by depressing the calcium and phosphorus metabolism, for it keeps children indoors away from sunlight, often alters the diet in ways which might favor the development of rickets and interrupts or stops altogether the administration of vitamin D. Experience with experimental rickets in rats, on the other hand, shows that complete starvation ends the rachitic disturbance. The fact that starvation induces deposition of calcium and phosphate in rachitic rats was pointed out years ago by McCollum, Simmonds, Shipley and Park.[6] In

6. McCollum, E. V.; Simmonds, N.; Shipley, P. G., and Park, E. A.: Studies on Experimental Rickets: XV. The Effect of Starvation on the Healing of Rickets, Bull. Johns Hopkins Hosp. **33**:31, 1922.

unpublished experiments on rats by Jackson and Park it was demonstrated that when the Steenbock and Black rickets-producing ration was reduced to 2 Gm. per day the picture of rickets was rapidly replaced by osteoporosis. The moment that sickness causes the individual to live on his own tissues, the inorganic phosphorus level of the serum rises and the rickets heals. The question why the prevalence was greater in the children dying of acute than in those dying of chronic illness is obviously too complicated for analysis.

We were unable to demonstrate any relationships between rickets and particular diseases with the exception of chronic lead poisoning, in which it was possible to think that the constant passage of lead through the alimentary tract might reduce the absorption of phosphate. In the literature on experimental rickets it has been shown that strontium,[7] iron,[8] magnesium,[9] beryllium [10] and other heavy metals all can produce rickets if fed in large enough quantities to form poorly soluble phosphate compounds in the alimentary tract. Further studies may bring out a relationship between rickets and certain diseases, but our studies with small groups failed to show association.

This problem of the relationship of the terminal illness to the rickets has great importance from the point of view of interpretation of our results and an equal importance never before suggested for those of Schmorl. To what extent was the illness from which the child died responsible for the rickets? In other words, can the results of our studies of the incidence of rickets in sick children be applied to healthy children? It can be seen in table 3 that about 50 per cent of the children dying from acute disease had moderate or advanced rickets. The degree of rickets in these children was greater than we believe could have developed in fourteen days or less, and we must conclude that these children had rickets before the onset of the acute illness. Schmorl's data and ours show definitely that rickets occurs commonly in sick children and thus suggest that it occurs commonly in children otherwise healthy. We wish, however, to make it clear that our studies do not imply that rickets occurs in approximately half of all children, since they deal with an analysis of a hospital population, not of the population at large.

It is interesting that in our studies the prevalence of rickets continued undiminished to the fourteenth year. Theoretically it does not seem remarkable that rickets should have been found so frequently in our older children, especially when it is found so commonly in infants, because in the case of older children administration of vitamin D is usually omitted entirely. We assume from our work that disturbances in calcium-phosphate metabolism must be very common in children, and it is evident that these disturbances quickly manifest their presence by detectable changes in the growing skeleton. The histologic method for detecting rickets is extremely delicate.

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We doubt if slight degrees of rickets, such as we found in many of our children, interfere with health and development, but our studies as a whole afford reason to prolong administration of vitamin D to the age limit of our study, the fourteenth year, and especially indicate the necessity to suspect and to take the necessary measures to guard against rickets in sick children.

CONCLUSIONS

Two hundred and thirty children aged between 2 and 14 years who died in the Harriet Lane Home from all causes were examined in consecutive autopsies for rickets.

The total prevalence of rickets was found to be 46.5 per cent. The figures according to years indicate that the disease occurred with scarcely diminished frequency up to the fourteenth year. In 23 per cent of the total number studied the disease was classified as slight, in 18.7 per cent as moderate and in 4.8 per cent as advanced.

In the white children the total prevalence was 43.6 per cent and in the Negro children 48.5 per cent. However, the prevalence of moderate and of advanced rickets taken together was 27 per cent in the Negro as compared to 18 per cent in the white children, and advanced rickets was limited exclusively to the Negro children. Thus, although the total prevalence of rickets was not greater in Negro than in white children, the prevalence of the disease in well developed degree was greater among Negro children.

No definite relationship between the occurrence of rickets and any particular disease could be established, with the probable exception of chronic lead poisoning. However, the number of patients in any disease group was not sufficiently great to exclude other possible relationships.

The prevalence of rickets among the children dying of acute disease was greater than among those dying of chronic disease. The significance of this is not clear. Disease may favor the development of rickets or, on the other hand, interfere with or actually block its development.

The greatest prevalence of rickets was in the winter months, December to February; the lowest, in the autumn months, September to November.

It is most important to appreciate that our studies dealt with a hospital population, not with the population at large. However, 50 per cent of the children dying of acute disease (arbitrarily defined as of fourteen days' duration or less) showed moderate and advanced rickets. Since, in our opinion, the degree of rickets in these children was greater than could have developed in less than two weeks, we believe that the children must have had rickets before the onset of the acute illness. Thus, our study suggests strongly that rickets is a frequent occurrence in healthy-appearing children.

The histologic method for detecting rickets is extremely delicate.

It was possible to recognize the rickets by means of roentgen examination in at most 5 cases. This fact is not remarkable, since the characteristic roentgenographic signs are those which develop at the cartilage-shaft junction and changes there are apt to be confined to so narrow a stratum in children 3 and 4 years old, because of the slower growth, that they do not show clearly; in still older children the changes at the cartilage-shaft junction may not develop at all, even though the shaft may be the seat of advanced involvement. With at most 5 exceptions, then, the rickets in the older children of this report could have given no outward signs of its presence.

TYPHOID-PARATYPHOID VACCINE AND POLIOMYELITIS

JOHN A. TOOMEY, M.D.
AND
LINDA A. TISCHER, M.D.
CLEVELAND

In a previous experiment, 6 newly weaned baby Macaca mulatta monkeys were each inoculated subserosally with typhoid-paratyphoid vaccine in a typhoid-paratyphoid-colon bacillus filtrate (enteric toxin) over a period of five months before being inoculated with poliomyelitis virus. During the process of immunization rickets developed in these animals. This fact tended to complicate the experiments, since rachitic monkeys are known to succumb quickly to poliomyelitis virus when it is given subserosally.

It is our experience that 0.5 cc. of a 1 per cent suspension of poliomyelitis virus when injected intracerebrally causes quadriplegia to develop in any macaca mulatta monkey but that this dose injected elsewhere is ineffectual. Poliomyelitis virus, then, is only relatively infective, and its effect depends in great measure on the portal of entry used. It is especially difficult to infect an animal by way of the subserosal portal, and in the previous experiment referred to the question of a proper dose was a problem. If massive amounts of virus were injected, all of the animals might simultaneously become paralyzed and no comparison could be shown. A 1 per cent suspension of virus in an amount which would not paralyze healthy monkeys when inoculated subserosally had been used, since such a concentration might produce some comparative results when these more susceptible animals were inoculated. The disease developed more quickly in the 6 rachitic baby monkeys that had been immunized with typhoid-paratyphoid vaccine and inoculated with this percentage of virus suspension than in healthy animals inoculated at the same time. The incubation time was found to be shorter, too, in the animals given subserosal injections, and the disease produced was massive and virulent.

It was decided to repeat the experiment previously mentioned, this time feeding the animals vitamin D to rule out the possible effect of rickets. We were not able again to secure a sufficient number of newly weaned baby monkeys to make the experiment, and the few that were obtained died while being prepared; hence older animals had to be used.

Twelve monkeys were divided into three groups of 4 animals each. The average age of those in group I was from 1 to 1½ years. During March and April 1942 they were fed a diet of apples, oranges, bananas, carrots, white rice and white bread soaked in whole milk. In addition, they received daily 1 mg. of thiamine hydrochloride and 5 drops of carotene in oil as well as 2 drops of viosterol in oil twice weekly. They were inoculated subcutaneously with 0.25 mg. of a standard typhoid-paratyphoid A and B vaccine every five days for six doses. One animal died of bronchopneumonia and intestinal infection before the completion of the immunization.

The average age of the animals in group II was from 1 to 1½ years. They were fed the same diet as those in group I but were not immunized with typhoid-

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From the Division of Contagious Diseases, City Hospital, and the Department of Pediatrics, Western Reserve University.

paratyphoid vaccine. The average age of the animals in group III was approximately 3 years. They were used to demonstrate the presence of virus in the suspension used.

Two weeks after the last inoculation of typhoid-paratyphoid vaccine we began to inoculate the animals with virus, 1 animal each from groups I, II and III receiving an injection on each of three succeeding days. A weak suspension of virus injected subserosally causes paralysis in a rachitic monkey very quickly. We have found this corollary to be true: A stronger suspension of virus is needed to paralyze a nonrachitic animal. The dose used was 70 cc. of a 10 per cent suspension of pooled unpurified monkey's cord virus diluted in a typhoid-paratyphoid-colon bacillus filtrate (enteric toxin).[1] It was injected subserosally into animals of groups I and II. The animals in group III received 0.5 cc. of the same preparation of virus intracerebrally. Flexner's M.V. strain, a virulent subtransfer received from Dr. Sabin, of the University of Cincinnati, was used.

As previously stated, 1 animal in group I died during the process of immunization. The first animal in group II died on the day of the operation from acute postoperative dilatation of the stomach; another animal was substituted. The first animal inoculated in group III was so sickly at the start of the experiment that it was felt that it would not survive. Although it did live, another animal from the same group had already been substituted. When the experiment was completed, there were 10 animals—3 in group I, 3 in group II and 4 in group III.

The animals were observed for clinical symptoms of poliomyelitis. All 10 acquired the disease. At autopsy, the cords and brains were removed and the sections were stained with hematoxylin and eosin.

RESULTS

The 3 animals that were immunized with typhoid-paratyphoid vaccine became weak and severely and mortally ill within two days after the injection of virus. One had a segmental type of palsy of the muscles in the legs. All 3 died of a severe fulminating disease—1 on the third and 2 on the fifth postinoculation day.

Histologic examination of the cord at all levels showed practically complete destruction of the cells of the anterior horn, pronounced hyperemia, fine hemorrhagic exudation and extensive neuronophagia—a typically severe type of reaction somewhat similar to that seen by Tupa[2] in patients who died of fulminating poliomyelitis.

Of the 3 nonimmunized animals in group II, 1 died of pulmonary tuberculosis on the nineteenth day. It had generalized weakness. In the 2 remaining only local paresis developed, affecting a few muscles of the left leg of 1 and the muscles of both legs and the right toes of the other. They were neither severely nor mortally ill at any time and would have lived but were killed on the twenty-first day. There were pathologic changes present that were not so severe in extent as but were similar to those found in the animals of group I. In addition, the animals of group II showed a late secondary change that occurs in human poliomyelitis, i. e. perivascular infiltration. The pathologic picture was out of all proportion to the mildness of the clinical symptoms. There was no positive pathologic evidence of poliomyelitis in the animal that died of acute dilatation of the stomach.

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2. Tupa, A.: Etudes histo-pathologiques dans la poliomyélite humaine et expérimentale du singe, Arch. roumaines de path. exper. et de microbiol. **7**:437, 1934.

All of the animals in group III came down with quadriplegia—1 on the sixth, 1 on the seventh and 2 on the eighth postinoculation day. These animals did not appear to be severely ill and ate well. They were nevertheless killed—1 on the eighth and 2 on the tenth day. The pathologic reactions were similar to those seen in group I, with the additional presence of perivascular infiltration.

COMMENT

We had thought that typhoid-paratyphoid vaccine injected into a rachitic monkey would heighten its susceptibility to poliomyelitis. The animals in group I, however, were not deficient in vitamin D. How can these divergent facts be explained? The end effect of severe rickets in the monkey and that of injections of typhoid-paratyphoid vaccine may possibly be the same, i. e., a depletion of normal antibodies against the enteric group of organisms. We have no evidence on this point. We do know, however, that there is a depletion of agglutinins against the enteric group of organisms in the experimental animal when it contracts poliomyelitis.[3]

In a recent communication Sabin, Ward, Rapoport and Guest[4] concluded: "There was no evidence that the capacity of poliomyelitis virus to invade the central nervous system along peripheral nerves depended on vitamin D deficiency." They inoculated monkeys intrasciatically whether the animals were deficient in vitamin D or not deficient and all of them acquired the disease.

This was in direct contrast to the results obtained by us in 1940 and by Harrison and Woolpert.[5] We later secured some of the Flexner M.V. strain carried by Sabin and found it an extremely virulent one, which paralyzed 100 per cent of our animals when injected intrasciatically. This confirmed the results of Sabin and co-workers.[6] We repeated our experiments with our laboratory strain of Flexner M.V. virus, and again none of the 3 animals inoculated intrasciatically came down with the disease. Harrison and Woolpert's results were similar to ours with the laboratory strain. They probably should be, since, according to the available evidence, both of us probably used the same substrain of Flexner's M.V. virus, obtained from the University of Chicago.

An explanation of the divergent results seems obvious. A difference in the quantitative efficacy of a strain may develop in different laboratories, as evidenced by our experiences. The subtransfer of the Flexner M.V. strain fresh from passage that was used by Sabin was virulent enough to paralyze 100 per cent of the monkeys when given by intrasciatic injection. It probably was so virulent that nothing would prevent a positive "take" unless the virus were directly neutralized by specific antiserum. The Flexner M.V. strain from the University of Chicago, kept in glycerin, which was used by us and probably by Harrison and Woolpert, was impotent when the sciatic nerve was used as the portal of entry. However, it still paralyzed all monkeys inoculated intracerebrally.

In some previous experiments our weaker strain was injected into the adrenals of 8 monkeys fed vitamin D, and there was no reaction. When broth toxins of

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4. Sabin, A. B.; Ward, R.; Rapoport, S., and Guest, G. M.: Neuroinvasiveness of Poliomyelitis Virus in Relation to Vitamin D Nutrition, Proc. Soc. Exper. Biol. & Med. **48**:451, 1941.

5. Harrison, S. A., and Woolpert, O. C.: Intraneural Injections of Serum as a Barrier to Migration of Virus in Experimental Poliomyelitis, J. Infect. Dis. **65**:214, 1939.

6. Toomey, J. A., and Takacs, W. S.: The Spread of Poliomyelitis Virus Along Axons of Peripheral Nerves, Am. J. Dis. Child. **63**:467 (March) 1942.

colon bacilli were added to this weak virus to bolster its virulence and it was then injected into the adrenals of vitamin D–fed monkeys, 1 had paresis and 1 quadriplegia; 6 remained well. When 8 more monkeys (4 vitamin D–fed and 4 vitamin D–deficient animals) were inoculated in like fashion, quadriplegia developed in all 4 of the vitamin D–deficient animals, while only 1 of the vitamin D–fed animals had but slight paresis and 3 were never ill at any time.[7] These clearcut results indicated that something did stop the spread in the vitamin D–fed animals—something probably not present in the vitamin D–deficient animals. Since myelin is affected in vitamin D deficiency, one might still postulate that deficient medullation permits a spread along peripheral nerves. The experiments of Sabin and coworkers do not contradict such a postulate.

One might theorize further and suggest that there are two conditions to be considered—some factor of local resistance to the spread of virus contained in the nerve myelin itself and a generalized coincidental lessening of the animals' antibodies. In this connection, it would be interesting to note whether monkeys immunized with typhoid-paratyphoid vaccine would acquire poliomyelitis more quickly than would the controls if inoculated with our weak Flexner M.V. strain.

Feeding of vitamins could not be an aggravating factor, since both groups of animals were given the same preliminary care.

It cannot be assumed that human beings and monkeys must have vitamin D deficiency, either actually or subclinically, to contract this disease. We merely have theorized that myelin protects the nerves; that it might possibly stop the spread of virus, and that one way to make myelin deficient in the Macaca mulatta monkey is by producing rickets in this animal. That there may be other ways of depleting this animal's natural resistance is obvious from the results of these experiments.

CONCLUSION

In a previous experiment, vitamin D–deficient Macaca mulatta monkeys immunized with typhoid-paratyphoid vaccine and later subserosally inoculated with virulent poliomyelitis virus became ill more quickly than did nonrachitic and nonimmunized animals. In the present experiments, nonrachitic but typhoid-paratyphoid–immunized animals contracted poliomyelitis more quickly than did nonrachitic and nonimmunized control animals when the virus was injected subserosally.

The number of animals used was too small to allow us to state that such results would always be obtained, even though in our experiments they were definite and contrasting.

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7. Toomey, J. A.: Absorption of Poliomyelitis Virus by Possibly Deficiently Medullated Nerves, Am. J. Dis. Child. **60**:548 (Sept.) 1940.

DISPARITY BETWEEN ORAL AND RECTAL TEMPERATURES AFTER EXERCISE

JOSEPH BRENNEMANN, M.D.
LOS ANGELES

It is well known that temperatures taken by rectum run about 1 degree (F.) higher than those taken by mouth. It is also generally known that the body temperature may rise several degrees with exercise, the elevation varying directly with the amount or intensity of the exertion. It is apparently not widely known that exercise will cause the rectal temperature to go up several degrees while the oral temperature taken at the same time may remain unchanged, rise slightly or, as often, fall to a lower point. I have, indeed, never personally encountered any one familiar with this phenomenon. In what would seem an adequately large and representative series of observations, herewith presented, I have failed to find a single instance in which this disparity was not strikingly in evidence. The purpose of this paper is to present data on the disparity. The clinical implications will at once be obvious to every physician, notably to every one dealing with children.

My attention was first directed to this behavior many years ago by a brief statement, unsupported by evidence, in a German medical journal. Unfortunately, I cannot give credit to the author, as I do not remember his name or that of the journal.

My first observation was a casual one on a boy of 8 years who had been fully recovered for several days from a mild infection of the upper respiratory tract. The mother, a responsible woman, was requested to take the boy's temperature by mouth and by rectum and then to let him walk rather briskly for about two hours. The oral temperature rose during this period from 98.6 to 98.8 F.; the rectal temperature, from 99.4 to 101.6 F.

A second observation was made on a boy of 11 years who had contracted pulmonary tuberculosis about two years before. He had been kept in bed most of the time since then because of a "rectal temperature above normal" after any exercise. He was admitted to the Children's Hospital for observation. Physical examination revealed no abnormalities except that he was soft, flabby and fat. His reactions were negative to tests for undulant fever and coccidioidomycosis.

The roentgenogram showed several well calcified hilar lymph nodes. There was no other evidence of pulmonary involvement. He was kept in bed for four days in order that his normal oral and rectal temperatures when he was at rest could be determined. The former ranged from 98 to 99 F.; the latter, from 99 to 100.4 F. on two occasions, with an average of about 99.6 F.

Four identical tests were made on successive days, each consisting of the taking of his oral and rectal temperatures by the same trained nurse while he was still in bed and after he had dressed and walked around a city block. The results are given in table 1.

It will be noted that in two of four instances the oral temperatures dropped to a lower point after exertion and that the average increase in rectal temperature was 1.8 degrees (F.) while the increase in oral temperature was only 0.05 degree. A drop in rectal temperature to normal within thirty to sixty minutes, as shown in tests 3 and 4, occurred every time that observations were made on that point.

The parents were advised to let the boy get up, gradually at first for psychologic reasons, and to assume normal activities in a short time; they were requested to omit determinations of temperature as far as possible. Some months later I was informed that the boy seemed well in every way and was no longer treated as an invalid.

The objection may be raised that these were unusual reactions because of the preceding infection. Be that as it may, the rectal temperature of each patient advanced about 2 degrees, while the oral temperature remained practically unchanged. The question raised by this possible objection was easily answered by seeing what would happen to unquestionably healthy children under analogous conditions of exercise.

Dr. Ina Richter, of the Loma Feliz School at Santa Barbara, Calif., made this part of the investigation possible under ideal conditions. In a private school to which only children "free from all infection" are admitted, 7 children, varying in age from 8 years and 5 months to 9 years and 10 months, were all submitted to different degreees of exercise, all of approximately the same duration. These consisted of three types: (*a*) one and one-half hours of hiking; (*b*) one-half

TABLE 1.—*Oral and Rectal Temperatures of a Boy 11 Years of Age Before and After He Had Walked Around a City Block*

Test	Time	Temperature (F.)	
		Oral	Rectal
1	Before exercise	99.2	99.6
	After exercise	99.0	101.6
2	Before exercise	98.6	99.4
	After exercise	98.8	101.2
3	Before exercise	98.6	99.8
	After exercise	98.4	101.6
	½ hour later in bed	99.4	100.4
	½ hour later in bed	99.8	99.6
4	Before exercise	98.0	99.4
	After exercise	99.2	101.2
	½ hour later in bed	99.8	99.2
	½ hour later in bed	98.6	99.6

hour of unorganized play and one hour of dancing and (*c*) one hour of spontaneous play with or without thirty to forty-five minutes of horseback riding. Hiking seemed, obviously, the most strenuous type of exertion, and details will be restricted to this type of exercise. In each of the others, however, the result was the same in kind but less in degree; this demonstrated, as has the result of every other comparative test, that the rectal temperature rose to an amount proportional to the duration and/or the intensity of the exertion while the oral temperature remained nearly unchanged and wholly unpredictable. Both oral and rectal temperatures were recorded just before and just after each exercise. The results of the hiking experiment are shown in table 2.

It will again be noted that the oral temperature dropped four times out of seven and showed an average increase following exercise of only 0.1 degree (F.). The rectal temperature, on the other hand, showed an average increase of 1.8 degrees (F.). In one instance the rectal temperature rose 3 degrees (F.) while the oral dropped 0.6 degree (F.).

Interest in this subject was largely due to the peculiar vagaries so often encountered in taking, or being told about, the temperatures of children, especially in private practice. With the results so constant in the observations just recorded, even a pediatrician might well wonder whether adults at different ages would

show a like reaction to physical exertion. Tests were made on 3 adults. The results were even more startling than those observed for children, probably only, following the general rule, because the exertions were more strenuous.

The first subject was a man apparently in robust health and approaching the scriptural allotment of "three score years and ten." Three tests were made, not only to determine the effect of exercise per se, but again to note the results with different degrees of exertion. Unfortunately, no determinations of temperature were made immediately before the tests, as was done for the other subjects. However, several trials made at different times during the day while he was at rest never yielded an oral temperature of more than 98.6 F. and a rectal temperature of more than 98.9 F. All of the following temperatures were taken for four minutes and with the same thermometer.

TEST 1.—This consisted of one hour of strenuous work, largely lifting and carrying heavy objects. At the end of the hour the temperature by mouth was 98.3 F., and by rectum 102 F. Thirty minutes later the temperatures were 98.6 and 100.4 F.; after another thirty minutes, 98.6 and 99.4 F., and four hours later (8 p. m.), 98 and 98.9 F.

TABLE 2.—*Oral and Rectal Temperatures of 7 Children Before and After They Had Hiked for One and One-Half Hours*

Subject	Time	Temperature (F.) Oral	Rectal
D	Before hiking	99.4	99.8
	After hiking	99.8	101.2
E	Before hiking	98.8	99.6
	After hiking	98.6	101.0
N	Before hiking	98.6	98.2
	After hiking	98.0	101.2
E	Before hiking	98.0	99.0
	After hiking	99.4	101.2
J	Before hiking	99.0	99.4
	After hiking	98.9	100.6
L	Before hiking	98.8	99.2
	After hiking	99.2	101.0
N	Before hiking	98.6	99.0
	After hiking	98.0	100.3

TEST 2.—This consisted of half an hour's hard work with resulting temperature by mouth of 98.6 and by rectum of 100.6 F. This was immediately followed by forty-five minutes of hard work, with the following readings: 98 and 101.4 F.

TEST 3.—This consisted of two hours of moderate exertion with readings of 98 F. by mouth and 100.4 F. by rectum.

A final trial was made with 2 young adults who played a rather strenuous game of tennis for one hour and ten minutes. The temperatures were taken for three minutes just before and just after the play. For 1 subject the readings were as follows: before the game, 96.4 F. by mouth and 98.4 F. by rectum; after the game, 97.4 and 101.4. There was thus a difference of 4 degrees between the temperature by mouth and that by rectum after the game and a difference of 5 degreees between the initial oral and the final rectal temperature.

For the second subject the readings were the following: before the game, 97.2 F. by mouth and 98.8 by rectum; after the game, 96.4 and 101.8. The oral temperature dropped 0.8 degree while the rectal temperature rose 3 degrees.

In no single instance was there any discomfort such as would accompany a like temperature due to an infection.

COMMENT

From the foregoing observations one would seem justified in concluding that it is a general rule that the rectal temperature rises to a much higher point after exercise than does the oral; also that this differential amount of increase is directly proportional to the intensity of the exertion. Furthermore, the evidence goes to show that there is a negligible change in the oral temperature and that whatever direction the slight change may take is, as already stated, quite unpredictable. The question naturally arises: Why is there this disparity? It is axiomatic that the higher reading, that for the rectal temperature, more nearly represents the temperature of the body itself; also, that one must think of the oral temperature as lower rather than of the rectal as higher. The rectum is a fully closed cavity in which the mucous membrane and the feces, if present, fit snugly against the thermometer on all sides. "Nature abhors a vacuum." The mouth, on the other hand, is a fairly large air-containing cavity that is not fully closed, inasmuch as it communicates through the pharynx and the nose with the outer world. Its mucous membrane, too, can hardly be applied as fully and constantly against the thermometer as is that of the rectum.

This leaves quite untouched any explanation as to why the temperature by mouth does not follow just a little behind that by rectum as is commonly observed. Even more puzzling is the fact that the temperature by mouth dropped about as often as it rose. Some one to whom these data were presented suggested that perhaps the temperatures were influenced by "panting at the time they were taken." There was no panting or mouth breathing at the time. This does not, however, exclude the possibility, even probability, that there was such breathing shortly before the temperatures were taken in the subjects who indulged in strenuous exertion. The air passing over the mucous membrane and the resulting evaporation would naturally tend to cool it, and it would still be approximately as cool when the temperature was taken. This is supported by the observation whenever the test was made that the oral temperature rose to a higher point one-half hour after exercise. This, at least, suggests that whatever factor caused the temperature to remain low had been nullified and that the effect of exercise now manifested itself in a rise in the oral temperature up to or beyond the normal for that subject at that time.

A further explanation was suggested by a colleague, a physician, with whom these observations were discussed. If while a person is in the sitting or standing position one hand is extended above the head for a time and the other is allowed to hang, the veins in the lowered hand will become engorged and the hand will feel warm while the raised hand will become blanched and colder than before. All of the exercises here recorded were done in the erect position, and the idea that the mouth and rectum might present a situation somewhat analogous to that of the two hands is at least inviting. However, since no such wide difference between the oral and the rectal temperature exists when the subject is at rest in the erect position, one must assume that exercise brings about a significant redistribution of the blood in the two parts of the body. The increased flow of blood and the heightened pressure that accompany physical exertion naturally lead to a greater engorgement of the rectal mucosa, with its rich and more loosely supported venous supply, than of the oral. The lower situation of the rectum may be a contributing factor. In other words, it seems fair to conclude that the blood, which is the thing that determines the reading, is brought closer, more fully and more abundantly to the thermometer in the rectum than it is in the mouth and that this condition is enhanced by exercise, with a resulting greater disparity

between the two temperatures than that which exists when the body has been at rest. In short, after exercise the rectal temperature is that of the blood; the oral temperature is not.

While all of the factors that have been suggested probably enter into the picture, a more authoritative opinion can doubtless be furnished by a physiologist.

From a clinical standpoint there are two main implications inherent in these observations, one helpful and the other potentially dangerous if not carefully evaluated. The practicing pediatrician sees a fairly large number of children who are brought to him because of an afternoon rectal temperature of 100 to 100.5, even 101 F. While I was writing this paper, a mother told me that her 6 year old child had been greatly restrained for a period of four months because he had an afternoon rectal temperature of 100.3 F. after any exercise although "he seemed perfectly well in every other way." If no other cause can be found for the high temperature, the condition may be safely dismissed as normal.

The danger to which I have alluded lies in the fact that another cause may exist and that a serious condition may be overlooked. The specter of tuberculosis is always present; less often, that of undulant fever, and in some regions of the far West, that of coccidioidomycosis. In doubtful cases, if these and other conditions that are accompanied by fever can be excluded by clinical observation, by specific tests and, of almost equal importance, by determining that there is no significant elevation of temperature if the child is fully at rest for a time, then, and only then, and only in selected cases, may the somewhat hazardous advice so often given, "to throw the thermometer away," be justified. In the case of an older child who "seems perfectly well in every way" one may be tempted to say that the oral temperature is the safer and less disturbing of the two!

It must be emphasized that all of the observations here recorded were made on persons who were apparently in normal health and that no deductions from these are applicable to a person who has a fever due to an infection. Whether the oral and rectal temperatures would react during fevers as they do in health after like exercise is of hardly more than academic interest, and no attempt was made to determine that reaction for rather obvious reasons.

SUMMARY AND CONCLUSIONS

In 10 children and 3 adults, all apparently in sound health, whose rectal and oral temperatures were taken just before and just after different degrees of exercise, the rectal temperature rose from 1 to 4 degrees Fahrenheit while the oral temperature remained unchanged, rose slightly or as often dropped to a lower point. The rise in rectal temperature and the variation from the oral were directly proportional to the intensity of the exercise. Both temperatures returned to normal in thirty to sixty minutes. Theories are offered to explain the unequal reactions, and some of the clinical implications are discussed.

4614 Sunset Boulevard.

PHYSICAL MEASUREMENTS OF COLLEGE WOMEN*

RESULTS OF FOUR CONSECUTIVE YEARS OF STUDY

EVA G. DONELSON, PH.D.†
ST. PAUL
MARGARET A. OHLSON, PH.D.‡
AMES, IOWA
BERNICE KUNERTH WATT, PH.D.§
WASHINGTON, D. C.
MARY BROWN PATTON, M.S.‖
WOOSTER, OHIO
AND
GLADYS M. KINSMAN, PH.D.¶
URBANA, ILL.

Whether women of college age, young adults in the late teens and in the twenties, are continuing to grow during the four year period of their college course is a moot question. The two measurements that have been used commonly for the investigation of this problem are height and weight. Survey studies have been made in several regions of the United States, and each has yielded much the same result as the others. Bowles's [1] report on measurements of Wellesley College women, Gordon's [2] on Smith College students and Diehl's [3] comprehensive survey of women of Cornell University, Leland Stanford University, Michigan State Normal College, University of Minnesota, North Carolina College for Women, Smith College, University of Wisconsin and University of Texas have all indicated no consistent relationship between advance in age and measurements for stature and weight. On the other hand, Carter [4] in his study of old Americans, 61 from Pembroke and 158 from the University of Tennessee, observed a progressive increase in height with age. Successive age groups in these survey studies were comprised of inde-

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§ With the assistance of E. J. Meiller, P. Nutter and R. Tucker. Contribution No. 111, Department of Home Economics, Kansas Agricultural Experiment Station.

‖ Approved for publication by the Ohio Experiment Station, Wooster.

¶ Approved for publication by the Oklahoma Experiment Station, Stillwater. Portions of the work at the Oklahoma Station were completed by Dr. Williamina Armstrong, following Dr. Kinsman's transferral to North Carolina State College for Women, Greensboro.

1. Bowles, G. T.: New Types of Old Americans at Harvard and at Eastern Women's Colleges, Cambridge, Mass., Harvard University Press, 1932.

2. Gordon, F. F.: Physical Measurements of 1,000 Smith College Students, Am. J. Pub. Health **20**:963, 1930.

3. Diehl, H. S.: Heights and Weights of American College Women, Human Biol. **5**:600, 1933.

4. Carter, I. G.: Physical Measurements of "Old American" College Women, Am. J. Phys. Anthropol. **16**:497, 1932.

pendent samples of the population. Barber and Stone [5] and Gould [6] have suggested that, whereas survey studies of college women yield little evidence that they are growing, measurements taken serially, whereby each student is observed annually and the composition of each age group consequently remains the same throughout the four years, demonstrate growth in height and in weight. Young [7] in an earlier study on 50 women whom he observed at ages 18, 19 and 20 years also found the students to show an increment in height with advance in age.

Hrdlička [8] concluded from his extensive work on adults that growth has not ceased by 22 to 24 years but proceeds slowly in some measurements to the fourth decade, in others to the fifth and, sometimes, even later. He noted that not all of the parts advanced at an equal rate and for the same period of time and that there were wide individual variations. A progression in the average figures for height was noted to extend well into the fourth decade; depth of the chest increased throughout most of the adult existence.

The current study, in which the measurements were taken serially, contributes data to the little explored terminal phase of physical growth in women.

PROCEDURE AND RESULTS

Measurements of height, weight, breadth and depth of the chest, circumference of each arm and of the left leg and grip pressure measurements of each hand of 209 women students were made annually during the four years of their college attendance. The series of measurements was recommended by Dr. Hrdlička and is described in an earlier publication.[9] The students observed were from the states of Iowa, Kansas, Minnesota, Ohio and Oklahoma.

In order to ascertain if there was a tendency of any of the measurements to show a progression with age, means and standard deviations were computed on the data, sorted according to the subjects' ages at entrance to college (table 1). It can be observed that there is no consistent change over the four year period in any of the measurements with the exception of height. The increment in this measurement persisted whether the student entered at age 17, 18, 19 or 20 years. The mean increase in stature for these ages, respectively, was 1.2, 0.4, 0.4 and 0.5 cm. To determine if growth in height of the magnitude indicated by these means would be significant, analyses of variance were computed.[10] The results of these analyses, recorded in table 2, indicate that the mean increase in stature for the four year period was significant for each group.

In addition, it was of interest to explore the character of this growth. To investigate the pattern followed by the means of the height measurements for the successive years of study, the mean squares for that variable were divided into the linear component and deviations from linear.[11] The linear component was found

5. Barber, R. G., and Stone, C. P.: Growth in Height and Weight in College and University Women, Science **83**:59, 1936.

6. Gould, H. N.: The Physique of Women Students at Newcomb College of Tulane University: I. Stature and Weight, Research Quart. Am. Phys. Educ. A. **1**:1, 1930.

7. Young, M.: Age of Full Stature in the Female and Epiphyseal Union of Long Bones of Lower Limbs, Am. J. Phys. Anthropol. **12**:285, 1928.

8. Hrdlička, A.: Growth During Adult Life, Am. Phil. Soc. Proc. **76**:847, 1936.

9. Donelson, E. G.; Ohlson, M. A.; Kunerth, B.; Patton, M. B., and Kinsman, G. M.: Anthropometric Data on College Women of the Middle States, Am. J. Phys. Anthropol. **27**:319, 1940.

10. Snedecor, G. W.: Statistical Methods, ed. 3, Ames, Iowa, Iowa State College Press, 1940.

11. Goulden, C. H.: Methods of Statistical Analysis, New York, John Wiley & Sons, Inc., 1939.

TABLE 1.—*Means and Standard Deviations of Eight Physical Measurements of 209 Women for a Four Year Period*

Measurement	Year	Entered at 17 Years			Entered at 18 Years			Entered at 19 Years			Entered at 20 Years		
		No.	Mean	Standard Deviation	No.	Mean	Standard Deviation	No.	Mean	Standard Deviation	No.	Mean	Standard Deviation
Height, cm.	1	20	163.8	5.28	94	164.8	5.31	74	164.7	5.92	21	162.9	4.39
	2	20	164.5	5.66	94	165.0	5.61	74	164.9	6.33	21	163.2	4.50
	3	20	164.8	5.86	94	165.0	5.56	74	165.0	6.79	21	163.2	4.27
	4	20	165.0	5.60	94	165.2	5.40	74	165.1	6.79	21	163.4	4.24
Weight, Kg.	1	20	56.3	5.60	94	58.5	7.44	74	59.3	8.61	22	57.2	7.18
	2	20	57.0	6.41	94	59.0	7.85	74	59.5	9.24	22	58.3	7.00
	3	20	56.8	6.62	94	59.2	8.08	74	58.8	8.46	22	57.1	7.04
	4	20	56.6	5.91	94	59.6	7.83	74	59.4	8.45	22	56.6	7.08
Breadth of chest, cm.	1	20	25.7	1.48	95	26.1	1.72	74	26.0	1.64	22	25.0	1.22
	2	20	25.5	1.34	95	25.9	1.66	74	25.8	1.87	22	25.3	1.35
	3	20	25.2	1.02	95	25.8	1.65	74	25.8	1.52	22	25.0	1.45
	4	20	25.2	0.93	95	25.9	1.73	74	25.9	1.45	22	25.0	1.43
Depth of chest, cm.	1	20	18.3	0.98	95	18.6	1.53	74	18.7	1.59	22	18.3	1.60
	2	20	17.9	1.00	95	18.4	1.57	74	18.6	1.65	22	18.3	1.52
	3	20	17.5	0.86	95	18.5	1.50	74	18.6	1.51	22	18.5	1.28
	4	20	18.3	1.00	95	18.6	1.33	74	18.8	1.57	22	18.9	2.37
Girth of right arm, cm.	1	20	26.2	2.20	95	26.7	2.35	73	27.2	2.46	22	27.0	2.44
	2	20	26.2	2.37	95	26.7	2.41	73	27.0	2.48	22	27.8	2.95
	3	20	26.0	2.53	95	26.7	2.68	73	26.7	2.40	22	27.0	2.44
	4	20	26.0	2.17	95	26.9	2.45	73	27.1	2.40	22	26.8	2.50
Girth of left arm, cm.	1	20	26.0	2.17	95	26.2	2.39	73	26.7	2.51	22	26.7	2.46
	2	20	25.8	2.34	95	26.2	2.37	73	26.6	2.58	22	26.9	2.25
	3	20	25.6	2.65	95	26.2	2.66	73	26.2	2.40	22	26.6	2.41
	4	20	25.6	1.93	95	26.3	2.56	73	26.4	2.33	22	26.4	2.33
Girth of left leg, cm.	1	20	35.3	1.70	91	36.0	2.03	70	36.3	2.54	19	35.8	2.58
	2	20	35.7	1.77	91	36.1	2.03	70	36.2	2.50	19	35.9	2.00
	3	20	35.2	2.15	91	36.1	2.24	70	36.1	2.52	19	36.0	2.29
	4	20	35.1	1.56	91	36.3	2.27	70	36.0	2.77	19	35.8	2.42
Pressure, right hand, Kg.	1	20	31	5.76	95	32	4.75	71	32	5.15	22	33	4.07
	2	20	31	5.58	95	32	5.27	71	32	5.58	22	32	5.32
	3	20	34	4.07	95	33	4.84	71	32	5.05	22	32	6.22
	4	20	33	5.28	95	32	4.71	71	31	5.20	22	32	5.89
Pressure, left hand, Kg.	1	20	28	5.67	94	29	4.96	71	29	3.06	22	30	3.77
	2	20	28	5.86	94	28	5.01	71	28	5.06	22	31	4.72
	3	20	29	4.38	94	30	4.56	71	28	4.96	22	30	5.07
	4	20	28	5.24	94	29	5.38	71	28	5.63	22	29	5.35

TABLE 2.—*Analysis of Variance of Measurements of Height*

Sources of Variation	17 Years at Entrance		18 Years at Entrance		19 Years at Entrance		20 Years at Entrance	
	Degrees of Freedom	Mean Square	Degrees or Freedom	Mean Square	Degrees of Freedom	Mean Square	Degrees of Freedom	Mean Square
Students	19	136.219*‡	93	120.657*‡	73	176.411*‡	20	73.890*‡
Years of study	3	5.082*‡	3	3.013*‡	3	2.417*‡	3	0.563†‡
Linear component	1	14.660*§	1	8.458*§	1	6.879*§	1	1.090§
Deviations from linear	2	0.288	2	0.290	2	0.186	2	0.301
Students × years of study	57	0.420	279	0.286	219	0.241	60	0.202
Students × linear component	19	0.932*‖	93	0.346†‖	73	0.285†‖	20	0.252‖
Deviations	38	0.164	186	0.256	146	0.218	40	0.177
Total	79		375	.....	295	.....	83	

* Hightly significant.

† Significant.

Errors used for testing significance:

‡ Students × years of study.

§ Students × linear component.

‖ Deviations.

to be significant in the measurements of those students who entered at ages 17, 18 and 19 years, which indicates that the increments in mean stature accrued with considerable regularity for successive years (table 2). For all groups, with the exception again of those who entered at age 20, the linear component of the interaction between students and years of study [12] was significant, which is indicative that individual students differed in rate of growth in height during the time of the study.

That the amount of growth in stature previously accomplished by a person may influence the rate of increase in this measurement in the terminal phases of growth has been demonstrated by Gould,[13] who found that shorter women students, irrespective of age, grew slightly more while in college than did taller women. The height measurements in the current study were sorted into two groups, those that were less than the mean minus one standard deviation (158.5 cm.) and those that exceeded the mean plus one standard deviation (170.3 cm.). Although the mean increase in stature during the four years for the short students exceeded that of the tall by 0.4 cm., the difference was not sufficiently great to be significant ($P < 0.0891$).

The mean values for the weight measurements increased between the first and the second year of study with each age of entrance; between the other years the changes were variable. Despite the fact that the lateral and the anterior-posterior diameter of the chest may both be expected to increase in adult life,[14] that trend was not manifested in these young adults over a four year period. Similarly, the girth measurements of the right and left arms and of the left leg changed very little and showed no progression with age. With the pressure measurements little variation occurred from year to year.

SUMMARY

Measurements of height, weight, breadth and depth of the chest, girth of the right and left arms and of the left leg and pressure of the right and left hands were made for four successive years on 209 women of college age residing in the states of Iowa, Kansas, Minnesota, Ohio and Oklahoma. The height measurements only manifested a consistent increase during the four year period.

F. R. Immer, Associate Director, Agricultural Experiment Station, University of Minnesota, and Gertrude Cox, Head, Department of Experimental Station Statistics, North Carolina State College, made recommendations concerning the statistical treatment of the data.

12. This computation was carried out for individual students in the same manner as for the means of the group. It is of noteworthy value in affording a procedure for delineating the behavior of the individuals within the groups.

13. Gould, H. N.: The Physique of Women Students at Newcomb College of Tulane University: V. Increase in Stature at College, Based on Repeated Measurements of the Same Individual, Human Biol. **11**:220, 1939.

14. Hrdlička, A.: The Old Americans, Baltimore, Williams & Wilkins Company, 1925.

VARIATION IN DIPHTHERIA ANTITOXIN TITERS OF HUMAN SERUM

REPORT OF AN EXTENDED STUDY, WITH SPECIAL REFERENCE TO AN ENDOCRINE AND VITAMIN RELATIONSHIP

MARY M. SCHMECKEBIER, M.D.*
SAN FRANCISCO

The literature records few determinations at frequent intervals of the diphtheria antitoxin titer of the blood serum of the same person over a period of several years. In 1925 Hamburger [1] reported a study of 6 subjects on whose blood serum antitoxin determinations were done on several occasions. No more than five determinations were done on any 1 subject, and the longest interval between the initial and the final determination of the antitoxin titer was one and one-half years. In 1 subject there was an increase in the antitoxin titer from 0.01 to 0.75 unit per cubic centimeter within two and one-half months without any apparent stimulus. In the other subjects there was considerably less variation. In 1929 Fitzgerald [2] published a paper on variations in the antitoxin content of serums of 6 adults over periods of from one to six years. In this article the amount of antitoxin in the serum of 3 subjects is expressed as less than 0.002 unit per cubic centimeter. The titer of antitoxin of the other 3 subjects is expressed as less than 2 units or more than 1.5 units per cubic centimeter. According to these results Fitzgerald concluded that over a period of about two years persons whose blood serum contains about 0.1 unit of antitoxin have no significant change in titer and that the titer of persons in the group with 0.002 unit or less per cubic centimeter does not fluctuate materially in antitoxin content. He found that in subjects whose level of antitoxin is 1 unit or more per cubic centimeter there may be variations from 1.5 to 2.5 units per cubic centimeter. In 1935 Neill and associates [3] reported the variations of the diphtheria antitoxin titer of 42 adults, all of whom had natural titers above 2 units per cubic centimeter. Some of the subjects were followed for only one year and others for as long as six and one-half years. In this select group, whose level of antitoxin represents that found in about 1 per cent of the general population, they found that 24 of the 42 adults maintained their antitoxin within levels such that the lowest titer observed at any time was never less than 50 per cent of the highest titer. This group is not comparable with the group of subjects reported on in this paper.

The object of the experimental work reported here was to follow at frequent intervals the diphtheria antitoxin titers of a group of women who were kept under close observation and for whom accurate histories were kept during the course of the experiment. The 9 subjects whose diphtheria antitoxin immunity is reported were mostly nurses, interns and residents from the Children's Hospital. There was diphtheria antitoxin in the blood serum of 3 of the subjects for whom there was no

* E. Charles Fleischner Endowment Fund Fellow.
From the Children's Hospital and the George William Hooper Foundation for Medical Research of the University of California.

1. Hamburger, F.: Hemoclinical Status, Monatschr. f. Kinderh. **29**:715 (March) 1925.
2. Fitzgerald, J.: Further Consideration of Question of Variation in Diphtheria Antitoxin Content of Blood of Adults, Tr. Roy. Soc. Canada (Sect. 5, Biol.) **23**:155 (May) 1929.
3. Neill, J. M., and others: The Individual as a Factor in Antidiphtheria Immunity: Adult Persons with High "Natural Levels" of Antitoxin, Am. J. Hyg. **21**:571 (May) 1935.

history of a previous diphtheritic infection or immunization. The other 6 subjects had been immunized against diphtheria. They were all women whose ages varied from 18 to 38 years. Six were followed for two years, with a minimum of 21 determinations and a maximum of 39 determinations of the antitoxin titer during this period of time. There were 13 determinations for 1 woman who was followed for eighteen months and 10 and 13 determinations respectively for 2 women who were followed for twelve months. In some cases specimens of blood were taken for a short period as often as every other day. From the history and study of the subject an attempt was made to determine any suggestive factor that seems to influence the level of diphtheria antitoxin in the blood serum of the subject.

EXPERIMENTAL PROCEDURE

Specimens of blood were usually collected before the morning meal, but at times, because of inability to communicate with the subject, it was necessary to take the specimen four and a half to five hours after a meal. The time the specimen was taken was recorded. The usual procedure was to obtain the initial determination of the titer within a week from the time the blood was taken from the subject. The serums were titrated concurrently for comparison and were checked on more than one occasion. (Several serums that remained perfectly clear and that were titrated again after standing in the refrigerator for a year in well stoppered sterile glass tubes with no preservative have shown little decrease in the antitoxin content during this period.)

Histories were kept of the time of the day the blood specimen was obtained, of any medication the subject was taking or had taken recently, of infections at the present time or in the interval since the previous determination, of the time of the menstrual cycle and of the general well-being of the subject, such as unusual fatigue or evident emotional reactions of any degree or duration. During the first eighteen months of the experiment no effort was made to influence the subject's regimen.

TECHNIC

The diphtheria antitoxin content of blood serum has been measured with considerable accuracy since 1909 by the use of the intradermal method. Romer [4] found that the intracutaneous injection of diphtheria toxin into guinea pigs produces a local area of inflammation characterized by varying amounts of redness, induration or necrosis, depending on the amount of toxin injected. This specific reaction is inhibited by a sufficient amount of antitoxin and can be used for the assay of toxin or antitoxin. As is well known, it is this reaction that is used in the Schick test and the Kellog test. In 1924 Fraser and Wigham [5] employed rabbits for the intracutaneous technic. By a further modification of this method Jensen [6] perfected a technic that made the determinations of antitoxin more accurate, and amounts as low as 0.0002 unit per hundred cubic centimeters of serum could be determined according to his method. This technic was substantially followed to obtain the experimental data that are here recorded.

With the ripened stabilized toxin used in the tests values lower than 0.001 unit per cubic centimeter were questionably accurate. This toxin maintained approximately 35 DRM in the LR/3,000 dose.[7] Three different standard antitoxins were used. They were of different

4. Romer, P.: Ueber den Nachweis sehr kleiner Mengen des Diphtheriegiftes, Ztschr. f. Immunitätsforsch. u. exper. Therap. **3**:208, 1909.

5. Fraser, D. T., and Wigham, H. E.: Use of Rabbits for Intracutaneous Virulence Tests of B. Diphtheriae or Titration of Diphtheria Antitoxin, J. A. M. A. **82**:1114 (April 5) 1924.

6. Jensen, C.: Die intrakutane Kaninchenmethode zur Auswertung von Diphtherie-Toxin und Antitoxin, Acta path. et microbiol. Scandinav., 1933, supp. 14, p. 1.

7. These units are taken from Jensen [6] (pp. 24 and 26), who defined them as follows: DRM represents the dosis reagens minima simplex: the arithmetical mean of at least three determinations on the same rabbit of the smallest amount of toxin which when injected

(Footnote continued on next page)

potencies and were frequently checked against each other. (The toxin and two different standard antitoxins were supplied by the Cutter Laboratories; the Lilly Research Laboratories supplied the other standard antitoxins.)

Large white mature male rabbits were usually used for the intracutaneous injections. Occasionally mature virgin female rabbits had to be employed. The cutaneous reactions to the toxin are more definite in the male but are usually not difficult to read in the female rabbit. In one instance forty-eight hours after the injections were made the cutaneous reactions were too indefinite to read, and the animal was found to be pregnant. In preparation of the rabbit the hair is removed from the back and sides with an electric clipper, and then a barium sulfide depilatory ointment is used. A petrolatum–hydrous wool fat salve is applied to the skin daily for a week prior to the time the injections are to be made. Except during the fall of the year little hair will grow back during this period. The depilated area can be divided into more than one hundred squares 2.5 cm. wide, the number depending on the size of the rabbit and on the amount of skin that is completely denuded after a week. The large number of titrations that can be tested on one rabbit is distinctly advantageous when numerous determinations are to be done at the same time. One-tenth cubic centimeter of each of the titration mixtures is injected intracutaneously in each test. Titrations are made up of decreasing amounts of various dilutions of serum and a constant amount of diphtheria toxin. Control

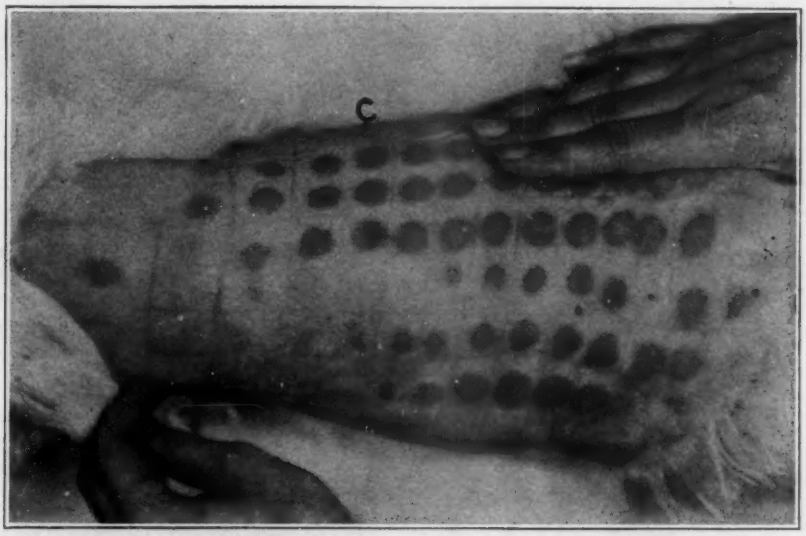

Fig. 1.—Cutaneous reactions forty-eight hours after injection of titrated unknown serums. *C*, control titration with known standard antitoxin.

titrations are made up of decreasing amounts of the standard antitoxin with the same amount of toxin that is used in titration of the unknown serums. The addition of the toxin and the process of mixing are uniform.

EXPERIMENTAL DATA

The levels of diphtheria antitoxin of the blood serum of the subjects of the experiment at different times are represented graphically in the following curves in figures 2 to 9.

Figure 2 presents the curves of 2 female interns, aged 24 and 26 years, who were studied over a period of one year. They both had reacted negatively to Schick tests, and neither had been immunized against diphtheria. Neither subject had a history that was suggestive

intracutaneously in a total volume of 0.1 cc. at p_H 7.4 produces a reaction which is visible after thirty-six hours as a clearly defined, weak inflammation 8 to 10 mm. in diameter. The LR/3,000 dose is the smallest amount of toxin which when mixed with an amount of a moderately rapidly reacting standard serum containing 1/3,000 antitoxic unit and allowed to stand for four hours at 37 C. causes a reaction corresponding to 1 DRM by intracutaneous injection into a rabbit in a total volume of 0.1 cc. at p_H 7.4.

of a previous diphtheritic infection. S. M. had a brother who had had diphtheria when they were children. She was an extremely emotional Jewish woman, who had an abundance of physical and nervous energy during the first few months of the experiment. She complained of being easily fatigued and of not feeling well most of the time for several months prior to the termination of the period of observation. No cause other than overexertion was found to explain the symptoms. During this period of five months the titer of antitoxin diminished from 1.15 units to 0.32 units per cubic centimeter. There was no suggestive correlation between the time of the menstrual cycle and the variation in the titer of this subject. The menstrual periods of A. B. were very irregular, with occasional intervals of several months between them. On several occasions the titer was higher two or three days prior to the onset

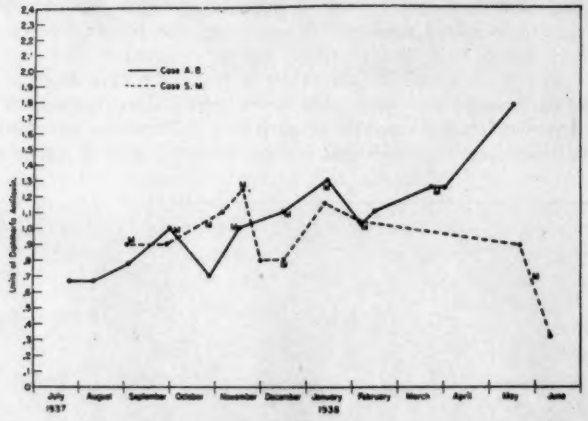

Fig. 2.—Antitoxin titers of A. B. and S. M. *M* on curves denotes time of menses.

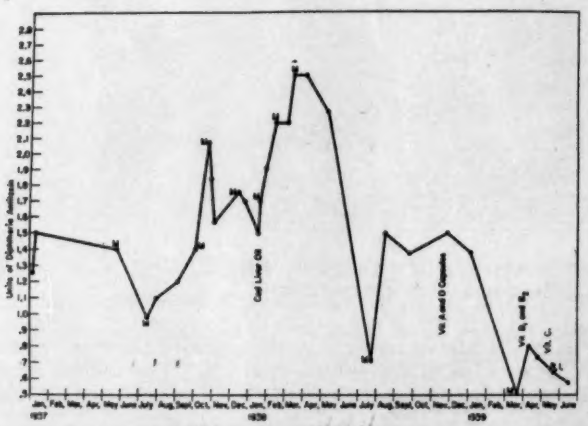

Fig. 3.—Antitoxin titers of a 37 year old woman physician. *R. I.* on curve indicates time of an infection of the respiratory tract.

of the period than it had been in the time between periods. She did not tend to overexert herself during her internship, and she seldom complained of her health. Her antitoxin titer increased from 0.67 to 1.3 units during the period of observation.

Figure 3 is the curve of a 37 year old single woman physician who had never been immunized against diphtheria and whose Schick reaction was pseudopositive just prior to the beginning of this study. She had frequently been in contact with persons with diphtheria over a period of years. In June 1937 her antitoxin titer was 1.4 units per cubic centimeter. In January 1938 the titer was 1.5 units per cubic centimeter. During that month she was vaccinated against smallpox, with a resulting immune reaction, and, being somewhat underweight, she started to take cod liver oil. By the middle of the following month the titer was 2.5 units per cubic centimeter. Thereafter there was a gradual decline in the titer to

0.5 unit one year later. During November 1938, when the titer was 1.5 units, vitamins A and D were taken again, in the form of a mixture of fish liver oils. One month later the titer was 1.38 units, at which time the vitamin capsules were discontinued. In April 1939 when the titer was 0.8 unit, the patient started to take vitamins B_1 and B_2 and took them rather irregularly, as vitamins A and D had been taken on both occasions. Additional vitamin B complex was taken for a period of eleven days, after which the titer was 0.73 unit. This vitamin preparation had to be discontinued because of abdominal distress and diarrhea during the therapy. One month later, when the titer was 0.64 unit, the subject took additional vitamin C, 100 mg. of ascorbic acid daily. Three weeks later the titer was 0.58 unit. There was no suggestive correlation between change in the antitoxin titer and the time of the menstrual cycle in this case. The periods were fairly regular.

The curve in figure 4 is that of a 30 year old married women who was a graduate nurse. Her Schick reaction was positive in 1933, and she was given 0.3 cc. of plain toxoid on August 17 of that year; two weeks later she was given 0.4 cc. and 0.5 cc. three weeks after the second injection. The Schick test elicited a negative reaction six months after the last injection. There was less variation in the titer of diphtheria antitoxin over a period of two years in the serum of this woman than in that of any of the other subjects reported on in this paper. The maximum amount of antitoxin was 0.56 unit, in August 1938, and the minimum amount was 0.2 unit, in February 1939. In December 1938 this subject took 18,400 U. S. P. units of vitamin A, and 3,400 U. S. P. units of vitamin D daily over a period of six weeks,

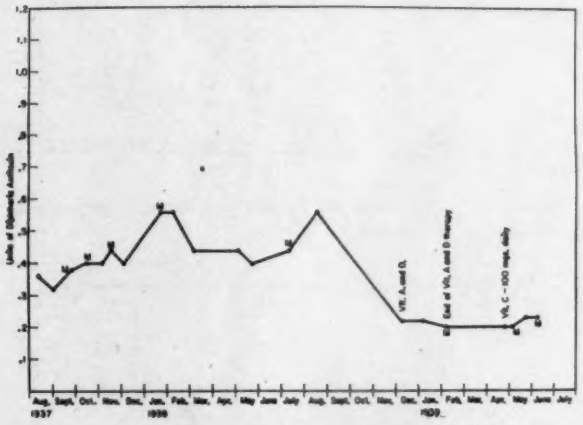

Fig. 4.—Antitoxin titers of a 30 year old married woman.

during which time there was little variation in the titer. In April 1939 she was given additional vitamin C, 100 mg. of ascorbic acid daily. Over a period of six weeks this had no appreciable effect on the titer. This subject seldom complained of her health; she usually had a carefree attitude, seldom showing any change of emotional status.

Figure 5 is the curve of a 30 year old single woman, a physician. This subject's Schick reaction was strongly positive in 1934, and she was given 1 cc. of alum-precipitated toxoid. This was followed by a severe local reaction. Six months after the injection of toxoid the Schick reaction was still strongly positive, leaving an area of discoloration for twelve subsequent months. In September 1936 plain formaldehyde-treated toxoid was given in amounts of 0.1, 0.2, 0.3 and 0.5 cc. with intervals of two weeks between the injections. No local or general reactions followed any of these injections. Three months after the last injection the titer of antitoxin in the blood was 1.72 units per cubic centimeter. Six months after the last injection of toxoid the titer of the blood was 0.63 unit per cubic centimeter. The variations in titer over a short period of time displayed by this woman were the greatest exhibited by any subject in this study. She was working in a hospital for patients with contagious diseases every day and frequently handled diphtheria toxin and toxoid. She was subject to all manifestations of allergy except severe asthma. She had frequent infections of the respiratory tract, gastrointestinal dysfunction accompanied with myalgia and arthralgia and neuritis with occasional elevation of temperature and increase in the white blood cell count during the course of the experiment. In the fall of 1939 she complained of pronounced fatigue that was accompanied by some emotional unbalance, and observations on her had to be discontinued. A diagnosis of chronic brucellosis was made. The minimum titer of diphtheria antitoxin

during the two years was 0.1 unit during January 1939, and the maximum titer was 1 unit during November 1937 and February and March 1938. The titer had decreased to 0.15 unit in September 1938, when the subject's hemoglobin content was found to be 58 per cent. During the next two months vitamins A and D and iron were administered, and the titer increased to 0.9 unit. The titer dropped to 0.1 unit three months later, and the use of vitamins and iron was resumed. In March 1939 the weekly administration of 20,000 international units of vitamin B_1 as thiamine hydrochloride intramuscularly produced no appreciable effect on the titer over a period of four weeks. Administration of this vitamin was discontinued when the subject had diarrhea and severe headaches and numerous herpetic lesions appeared on the face. There was no consistent variation during the menstrual cycle. The periods

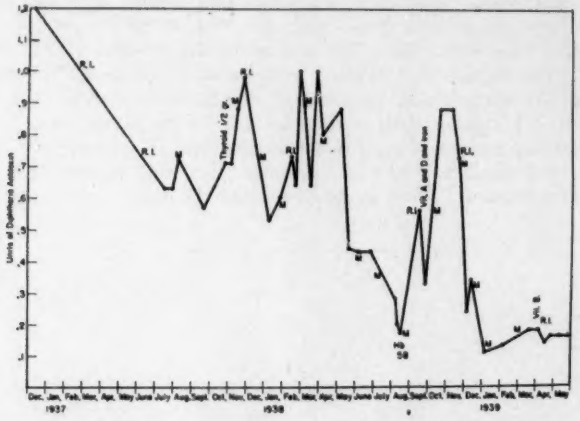

Fig. 5.—Antitoxin titers of a 30 year old unmarried woman physician. *R. I.* on curve indicates time of an infection of the respiratory tract.

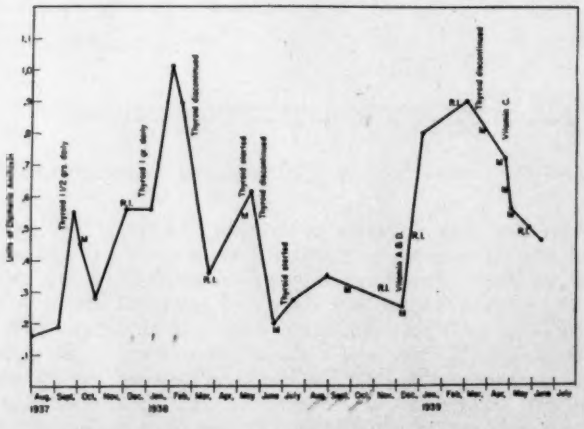

Fig. 6.—Antitoxin titers of a 20 year old unmarried student nurse with deficiency of thyroid function.

occurred regularly, every twenty-eight to thirty days, but flow was diminished in amount and duration during the last year of observation.

The next three subjects to be reported on were found to have some deficiency of thyroid function.

Figure 6 is the curve of a 20 year old unmarried student nurse. She was immunized in October and November 1936 with five small doses (0.1 to 0.3 cc.) of plain diphtheria toxoid that were given at weekly intervals. Her basal metabolic rate was —32 per cent in July 1937, and she had had no menses for eight months. The titer of diphtheria antitoxin at this time was 0.16 unit per cubic centimeter. Two months later, when the titer was 0.18 unit, she was given

1½ grains (0.1 Gm.) of thyroid daily. Three weeks after the taking of thyroid was started the titer was 0.55 unit per cubic centimeter. After taking thyroid for a month this subject had a normal menstrual period, and the antitoxin titer at the termination of the period was 0.28 unit per cubic centimeter. The use of thyroid was continued, and after three months the titer had increased to 1 unit per cubic centimeter. Then on three occasions there was a prompt decrease in the titer when she stopped taking thyroid for several weeks and a subsequent increase when the medication was resumed. In December 1938, when she took 18,000 U. S. P. units of vitamin A and 3,400 U. S. P. units of vitamin D besides 1 grain (0.06 Gm.) of thyroid daily, there was an increase in the titer from 0.25 to 0.8 unit after an interval of three weeks. Daily administration of 100 mg. of ascorbic acid in April 1939, at which time the administration of thyroid was discontinued, was accompanied by a decrease in the titer from 0.72 to 0.56 and then to 0.46 unit two months later, when the use of ascorbic acid was discontinued. At this time the basal metabolic rate of the subject was —20 per cent. Several cultures of material from the nose and throat of this subject yielded no Klebs-Loeffler bacilli during the course of this study.

Figure 7 is the curve of a 32 year old married female intern. She had had two injections of 0.5 cc. each of plain diphtheria toxoid with an interval of two weeks between the doses in 1934. The basal metabolic rate of this subject was —20 per cent in July 1937, at which time the diphtheria antitoxin titer was 0.02 unit. Three months later the titer was 0.31 unit. In February 1938 vitamin capsules with vitamins A and D were taken somewhat irregularly

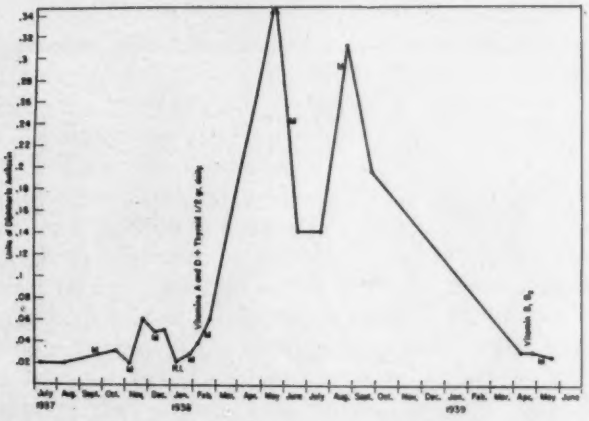

Fig. 7.—Antitoxin titers of a 32 year old married female intern with deficiency of thyroid function.

and ½ grain (0.03 Gm.) of thyroid was taken daily. During the time that this therapy was continued there was a gradual increase in the titer over a period of three months to 0.34 unit per cubic centimeter, which was seventeen times the original amount. The thyroid was then taken irregularly, and the use of the vitamin capsules was discontinued. The antitoxin titer diminished to 0.14 unit in July 1938 and then increased to 0.31 unit in September, after which there was a diminution to 0.032 unit. During April 1939 this subject was given 1,150 international units of vitamin B_1 and 90 Sherman-Bourquin units of vitamin B_2 daily for a period of four weeks. The antitoxin titer decreased from 0.045 to 0.032 unit per cubic centimeter during this period. This subject had some emotional instability. Her menses were very irregular. There was no suggestive correlation between the change in the titer and the time of the menstrual cycle.

Figure 8 is the curve of a 26 year old unmarried female intern. Her basal metabolic rate was —20 per cent in January 1938, when the first determination of diphtheria antitoxin was done on her blood serum. She appeared to have some endocrine dysfunction. Her Schick reaction was strongly positive in 1933, and subsequently she was given 0.1 cc. of plain diphtheria toxoid on Oct. 26, 1933 and 0.2 cc. one month later. Six months after the second injection of toxoid the Schick reaction was negative. In December 1937 the diphtheria antitoxin titer was 0.019 unit per cubic centimeter. At this time this subject started to take thyroid, which she continued to take rather irregularly for several months in doses that varied from ½ to 2 grains (0.03 to 0.13 Gm.) daily. One month after the beginning of the thyroid therapy the antitoxin titer was 0.036 unit per cubic centimeter. Two months after the second

determination it had decreased to 0.01 unit. Vitamins B_1 and B_2 taken in irregular amounts for four weeks during March 1939 had no apparent effect on the antitoxin titer. This subject was a hyperkinetic, emotional Jewish woman. She had extremely irregular menstrual periods during the course of this study. The periods did not seem to affect the fluctuation in the antitoxin titer.

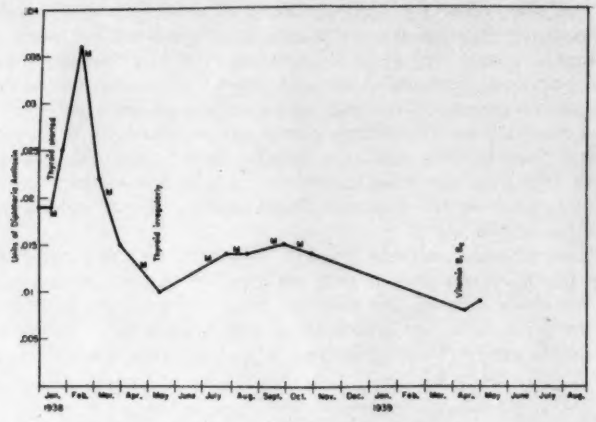
Thyroid started
Thyroid irregularly
Vitamin B1 B2
Jan. Feb. Mar. Apr. May June July Aug. Sept. Oct. Nov. Dec. Jan. Feb. Mar. Apr. May June July Aug.
1938
1939

Fig. 8.—Antitoxin titers of a 26 year old unmarried female intern with deficiency of thyroid function.

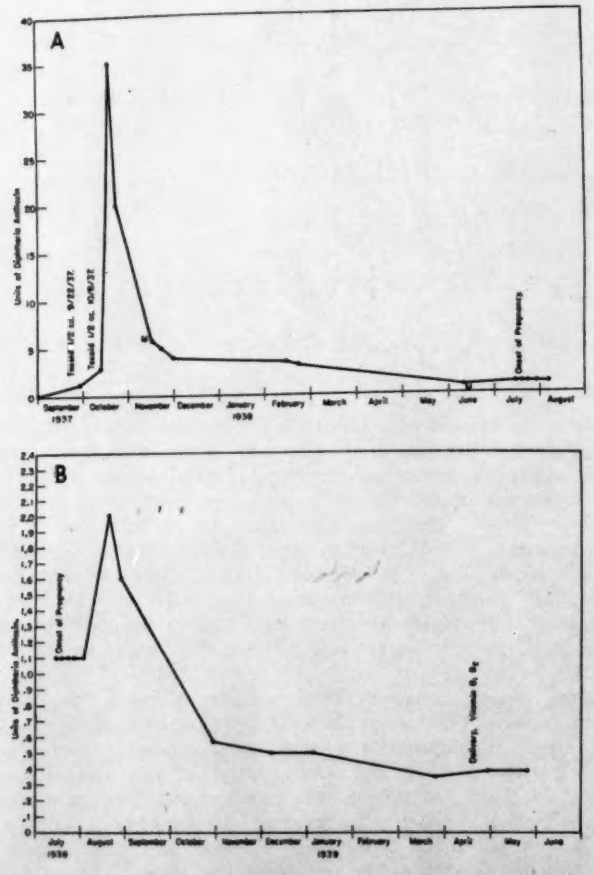

Fig. 9.—Antitoxin titers of a 26 year old married female intern. *A*, from September 1937 to August 1938; *B*, July 1938 to June 1939.

Figure 9*A* is the curve of a 26 year old married female intern. She had a positive Schick reaction in 1935, at which time she was given 1 cc. of alum-precipitated toxoid. Six months after this the Schick test still elicited a strongly positive reaction. In July 1937 the antitoxin titer of her blood was less than 0.001 unit per cubic centimeter. She was given 0.5 cc. of plain toxoid on Sept. 22, 1937, with no local or general reactions resulting. Titrations of serum antitoxin were done every other day. Four days after the injection of toxoid there was between 0.001 and 0.004 unit. By September 27, or five days after the initial injection, the antitoxin titer was 0.11 units per cubic centimeter. Two weeks after the first injection another 0.5 cc. of plain toxoid was given, with no resulting ill effects. The titer then rose rapidly during the following week to 35 units and then decreased, so that it was 1 unit six months later. The curve in figure 9*B* represents the diphtheria antitoxin immunity of the same woman from June 1938 to June 1939. Five specimens of blood were taken during July 1938, which showed no variation. The following month the titer had increased to 2 units, which was twice that of the previous month. Then a decrease in the titer followed. In January 1939 the reason for the subject's amenorrhea of the previous six months was revealed by the fact that she became pregnant during July of the previous year. It was during the first month of the pregnancy that the titer increased to two times that of the previous month. At the time of delivery in April 1939 it was 0.35 unit per cubic centimeter. Administration of vitamins B_1 and B_2 started three weeks after delivery and continued for one month had no apparent effect on the titer. There was 0.39 unit per cubic centimeter when the therapy was begun and when it was terminated.

COMMENT

The data presented in this paper are interesting so far as they show the amount of variation that may take place from time to time in the diphtheria antitoxin circulating in the blood serums of a group of women over a period of several years as well as suggesting some definite relationship between the immune mechanism and the endocrine function.

In considering the neutralization of diphtheria toxin by blood serum several substances other than diphtheria antitoxin must be taken into account, since they have been reported to neutralize or detoxify diphtheria toxin in vivo or in vitro. Among these are vitamin C, adrenal cortex hormone, sex hormones of the anterior lobe of the pituitary gland and the sterols, including cholesterol.[8] Since no determinations were done for any of these substances, it is possible that something other than diphtheria antitoxin may have been responsible for the neutralization of the toxin used in the determinations. The administration of additional vitamin C to the subjects did not seem to affect the fluctuation of the titer of antitoxin. Some variation in the hydration of the subjects may have influenced the results obtained. The neutralization or detoxification could not have been effected by a change of p_H, as the buffer solution used in the titrations maintained a p_H of 7.4 and the blood serum of normal subjects would vary little in p_H.

The relationship between the endocrine system, the vitamins and the immune mechanism has been discussed for a number of years, but as yet there are still few definite conclusions about it. Hormones have been referred to as one of the nonspecific mechanisms of defense. Clinically, physicians are aware of the increased resistance to certain types of infection during pregnancy as well as the decreased resistance to other types of infection, as has also been shown experimentally.[9] Perla and Marmorston stated the belief that it is possible that the increase in gonadotropin in the course of pregnancy may be one of the factors responsible

8. Eisler, M., and Gottdenker, F.: Ueber die Entgiftung des Diphtherietoxins durch Lanolin und Sternine, sowie über die Beeinflussung seines Immunisierungsvermögens durch Cholesterin, Ztschr. f. Immunitätsforsch. u. exper. Therap. **90**:427 (July) 1937.

9. Jungeblut, C.: Further Observations on the Poliocidal Property of Pregnant Mare Serum, Proc. Soc. Exper. Biol. & Med. **33**:137 (Oct.) 1935. Sprunt, T. P.: Some Recent Developments in Field of Endocrinology of Interest to General Practitioner, Virginia M. Monthly **59**:447 (Nov.) 1932; Infectious Myxomatosis in Pregnant Rabbits, J. Exper. Med. **56**:601 (Oct.) 1932.

for the alteration in the resistance to infection. This is increased mostly in the early months of pregnancy, and diminishes after the fifth month. The diphtheria antitoxin titer of the pregnant subject reported on in this paper increased during the early part of the pregnancy, so that during the sixth week the amount was twice that at the onset. There was then a decrease in the amount of antitoxin, so that at the termination of the pregnancy, after nine months, the level of antitoxin was approximately one third of what it had been at the onset of the pregnancy. Löwenthal [10] reported on a group of 240 pregnant women, of whom more than half showed an increase in the nonspecific agglutinins to Bacterium dysenteriae toward the end of gestation and during lactation. There was no evidence of recent infection or exposure to infection. Jungeblut and Engle [11] pointed out that poliomyelitis rarely occurs during the early period of pregnancy. They found that the virucidal titer of pregnancy serums is considerably higher than that of normal serums. Sprunt and Dearman [12] in experimenting with castrated male rabbits found that the resistance to infection with vaccinia is increased if the rabbits have been given large amounts of estrogen prior to the vaccination. These animals also recovered from their cutaneous lesions more readily than the controls. Weinstein [13] reported on the prophylaxis of experimental anthrax infections with various endocrine preparations. Magara [14] has shown that although the sex hormones decrease susceptibility to tetanus and diphtheria no increase in antitoxin can be determined. Lauber [15] infected mice with staphylococci, streptococci and pneumococci and found that if he injected an endocrine substance into the animals after the infection a large percentage survived, while the controls died.

The reports of variations in the immune properties of the blood serum during different times of the menstrual cycle are as conflicting and varying as the reports on the variation in the basal metabolic rate during different times of the menstrual cycle. There was no consistent variation in the subjects reported on in this experiment.

One of the better reports on the effect of vitamin deficiency on the immune mechanism is that of Jusatz.[16] He put growing rabbits on a diet that was made vitamin free by pressure cooking at 120 C. Besides their normal growth's being arrested they had subnormal bactericidal titers to Staphylococcus aureus. These deficiency rabbits were not able to produce specific precipitins. The subsequent addition of vitamins to the diet did not seem to cause any serologic benefits. He found that the oral administration of vitamins A, B, C and D to normal rabbits had no appreciable effect on the bactericidal titer of the blood serum. Madison

10. Löwenthal, W.: Erklärungsversuche für Ruhragglutination durch Schwangerenserum, Ztschr. f. Immunitätforsch. u. exper. Therap. **30**:439, 1920.

11. Jungeblut, C., and Engle, E. T.: The Influence of Pregnancy and of Menstruation on the Power of Normal Human Sera to Inactivate Poliomyelitis Virus, J. Immunol. **24**:267 (April) 1933.

12. Sprunt, D. H., and Dearman, S.: Studies on Relationship of Sex Hormones to Infection: Effect of Estrogenic and Gonadotropic Hormones on Vaccinia and Spreading Factor, J. Exper. Med. **67**:159 (Jan.) 1938.

13. Weinstein, L.: Prophylaxis of Experimental Anthrax Infection with Various Hormone Preparations, Yale J. Biol. & Med. **11**:369 (March) 1939.

14. Magara, M.: Sur le rôle anti-toxi-infectieux de l'hormone sexuelle, Compt. rend. Soc. de biol. **125**:779, 1937.

15. Lauber, H. J.: Innere Sekretion-Infektionsbereitschaft und Wundheilung, München. med. Wchnschr. **77**:434 (March) 1930.

16. Jusatz, H. J.: Der Einfluss der Vitamine auf den Immunitätszustand des tierischen Organismus, Ztschr. f. Immunitätsforsch. u. exper. Therap. **88**:472 (Aug.) 1936.

and co-workers [17] found that an excess of vitamin C in the diet of rabbits greatly enhances the formation of precipitins but causes a 60 per cent reduction in the average yield of specific agglutinins. Chu and Chow [18] found a qualitative relationship between vitamin C and complement titer in human plasma.

What part does thyroid formation play in the resistance to infection? Of the 9 subjects reported on in this paper, the 3 having the lowest basal metabolic rates (— 18 to — 32 per cent) had the lowest antitoxin titers. All 3 had been immunized in different ways. They showed various amounts of increase in the diphtheria antitoxin in the blood serum following thyroid therapy, while 2 of the other subjects in the group, with normal basal metabolic rates and no evidence of hypothyroidism, showed no suggestive response to thyroid therapy. In 1 hypothyroid subject on three occasions there was a prompt decrease in the titer of antitoxin after discontinuance of the use of thyroid for several weeks and a subsequent increase when the medication was resumed.

Fassin [19] in 1907 found that the subcutaneous injection and the feeding of thyroid to dogs and rabbits was followed by a rapid rise in the alexin content of the plasma. Removal of the thyroid gland was followed by a reduction of the alexin. Marbe [20] found that the administration of thyroid to normal rabbits was followed by an increase in the opsonic index of their serums. Brun [21] and Muller [22] also reported a rise in complement following the use of thyroid extracts. Stschedrowitzky, Korabelnikow and Lopatin [23] studied the effect of thyroidectomy and castration of rabbits on the agglutinin-building power of the blood and also on the formation of antitoxin. They found that shortly after thyroidectomy there was a decrease in the power of producing antibodies which was evident for as long as six months. After rabbits were castrated the agglutinin-building power of the blood diminished during the first two or three months following the operation. The feeding of thyroid to the thyroidectomized animals increased the antitoxin and the agglutinins of the blood. Houssay and Sordelli [24] observed that in horses thyroidectomized several years previously and immunized by repeated injections of toxin-antitoxin mixtures and pure toxin the antitoxin response was distinctly lower than in normal horses. They obtained similar results in rabbits but not in dogs. Eickhoff [25] reported a definite decrease in the capacity of thyroidectomized animals to form precipitins. The administration of thyroid enhanced the precipitin response.

17. Madison, R., and others: Vitamin C Inhibition of Agglutinin Production, Proc. Soc. Exper. Biol. & Med. **39**:545 (Dec.) 1938.

18. Chu, F. T., and Chow, B. F.: Correlation Between Vitamin C Content and Complement Titer of Human Blood Plasma, Proc. Soc. Exper. Biol. & Med. **38**:679 (June) 1938.

19. Fassin, L.: Influence de l'inoculation d'extracts thyroidiens sur les proprietes actives du serum, Compt. rend. Soc. de biol. **62**:388, 467 and 647, 1907.

20. Marbe, S.: Les opsonines et la phagocytose dans les etats thyroidiens, Compt. rend. Soc. de biol. **67**:44, 1909.

21. Brun, V.: Einfluss der Produkte des thyreo-parathyreoidealen Apparates auf die alexinischen Eigenschaften des Blutes, Centralbl. f. Bakt. (Abt. 1) **56**:533, 1910.

22. Muller, L.: Recherches sur le lieu et le mode d'origine des cytolysines naturelles (alexines et ambocepteurs normaux) et les moyens d'en provoquer l'hypersécrétion, Centralbl. f. Bakt. (Abt. 1) **57**:577, 1911.

23. Stschedrowitzky, S. G.; Korabelnikow, A., and Lopatin, E. K.: Ueber Die Rolle der Schilddrüse und Testes in der aktiven Immunität, Ztschr. f. d. ges. exper. Med. **72**:703, 1930.

24. Houssay, B. A., and Sordelli, A. J.: Sensibilite des animaux ethyroides envers les toxines et le bacille diphterique, Compt. rend. Soc. de biol. **85**:677, 1921.

25. Eickhoff, W.: Schilddrüse und Allergie (Experimentelle Untersuchungen über die Abhängigkeit der allergischen Reaktion vom Funktionszustand der Schilddrüse), Virchows Arch. f. path. Anat. **303**:481, 1939.

Rocchini [26] observed a favorable effect of thyroid extract on the formation of agglutinins against Bacterium typhosum. Hirschberg and Bronstein [27] reported on the immunization of a cretin with typhoid vaccine. The patient showed no response to typhoid inoculations in the absence of thyroid activity. After the administration of thyroid an antibody response was noted.

The possibility that persons may harbor Klebs-Loeffler bacilli that are not detected in a culture of material from the nose and throat, but which are responsible for antigenic stimulation at regular or irregular intervals must be considered in any case in which there is a great increase in the antitoxin content of the patient's serum.

SUMMARY AND CONCLUSIONS

The diphtheria antitoxin titer of the blood serum may fluctuate considerably in some persons. In 1 subject there was an increase to seventeen times the original amount over a period of four months. In another there was a variation from 0.6 to 1 unit per cubic centimeter within four days.

The results of this study suggest a definite relationship between thyroid function and the amount of diphtheria antitoxin present in the blood serum.

There is no suggestive correlation between the variation in the antitoxin content of the blood serum and the time of the menstrual cycle.

The administration of vitamins B_1, B_2 and C for several weeks did not seem to be accountable for any change in the antitoxin titer of the blood serum of the subject studied. Of 7 persons to whom vitamins A and D were given, there was considerable increase in the titers of 4 after several weeks. To 2 of these subjects thyroid was also given in conjunction with the vitamins. The possibility of increased enhancement of the immune response in hypothyroid subjects by the administration of vitamins A and D in conjunction with thyroid needs further study.

Drs. K. F. Meyer, H. E. Thelander and E. B. Shaw gave helpful suggestions and criticism during this experimentation.

2000 Van Ness Avenue.

26. Rocchini, G.: Azione dell'ormone tiroideo sui fenomeni della immunità antibatterica e della anafilassi, Boll. d. Ist. sieroterap. milanese **16**:551 (Sept.) 1937.

27. Hirschberg, N., and Bronstein, I. P.: Note on Cretins Response to Typhoid Inoculation, Am. J. M. Sc. **202**:333 (Sept.) 1941.

Case Reports

POIKILOTHERMIA IN AN ACHONDROPLASTIC DWARF

RESULTS OF MEASUREMENTS OF HEAT PRODUCTION AT VARIOUS TEMPERATURES

WALTER R. MacLAREN, M.D.
BOSTON
AND
OSCAR CORREA, M.D.*
SANTIAGO, CHILE

Poikilothermia may be defined as a state wherein the body temperature of an organism tends to approach at all times that of the surrounding medium. No thermostatic control from within is present to maintain a constant body temperature by increasing or decreasing heat production and storage as the environmental temperature changes.

A transient state of poikilothermia is occasionally observed in premature infants, but it seldom persists after the first week of life. It is usually regarded as a sign of immaturity of the central nervous system. Aside from this, poikilothermia in human beings is a rare condition. The only case that has come to our attention is that reported by Davidson and Friedman.[1] Their patient was an infant who during his twenty-nine days of life showed instability of body temperature, tremors, athetosis and xanthochromia of the spinal fluid. At autopsy the hypothalamic nuclei were found to be extensively invaded by a neuroblastoma.

The case here presented is that of a 3 year old achondroplastic dwarf with poikilothermia. His instability of body temperature was associated with stigmas of mental deterioration, which appeared when he was about 2 years of age.

REPORT OF A CASE

F. C. M., a white boy, was born Sept. 1, 1939, by breech extraction, after a full term normal primiparous gestation. His birth weight was 2,730 Gm. (6 pounds); his length was 47 cm., and he measured around head, chest and abdomen, respectively, 36.75, 32 and 36 cm. No abnormalities were noted. No family history of dwarfism was obtained. His father was said to have been of short stature and of normal proportions. His mother was 59 inches (150 cm.) tall, weighed 113 pounds (51.3 Kg.) and was well proportioned. The mother's Wassermann reaction was negative during and after pregnancy.

When he was 2 months of age, the patient showed typical signs of achondroplasia: short extremities, broad turned-up nose, "trident hand" with short fingers, prominent abdomen with diastasis recti abdominis and in addition a small chest, slight strabismus and poor muscle tone. The heel of the hand failed to reach the iliac crest by ½ inch (1.3 cm.). The center of the body fell 1½ inches (3.8 cm.) above the umbilicus. Chemical examination of the blood at this time showed: calcium, 10.7 mg. per hundred cubic centimeters; phosphorus, 6.4 mg.; serum phosphatase, 13.8 Bodansky units; sugar (fasting), 83 mg., and nonprotein nitrogen, 28 mg. per hundred cubic centimeters. The tuberculin and Hinton reactions were negative and have remained so since. His temperature was normal. The basal metabolic rate was + 84 per cent for his weight and height. He was doing well on a caloric intake of 110 to 120 calories per kilogram (50 to 55 calories per pound of body weight), and adequate amounts of vitamins C and D.

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* Fellow of the Rockefeller Foundation.
From the Children's Medical Service of the Massachusetts General Hospital and the Department of Pediatrics, Harvard Medical School.

1. Davidson, C., and Friedman, E. P.: Poikilothermia with Hypothalamic Lesions: A Clinicopathologic Study, Arch. Neurol. & Psychiat. **38**:1271-1287 (Dec.) 1937.

For two and one-half weeks anterior pituitary extracts containing the growth factor were given empirically without significant results.

When he was 9½ months of age, he weighed 6,690 Gm. (14 pounds 12 ounces) and except for two short bouts of fever associated with teething had been well. He had learned to sit up with support but was unable to control well his rather large head. His measurements were: length, 60.5 cm.; circumference of head, 45 cm.; chest, 38 cm., and abdomen, 43 cm. His eyes and vision were normal. He had two lower incisors.

Until he was 21 months old, he continued to do well physically. His weight increased to 8,600 Gm. (19 pounds); sphincter control was established; he had learned to say a few words; he ate sitting up, and he could walk if assisted. Then, without any discernible cause, he began to lose ground physically and mentally. He lost his ability to sit up, stopped using the few words he knew, lost sphincter control, took little interest in his surroundings and had a rise in temperature every few days.

On July 24, 1941, at the age of 22½ months, he was admitted to the wards of the Children's Medical Service at the Massachusetts General Hospital. He weighed 7,630 Gm. (16 pounds 13 ounces), and the circumferences of the head, chest and abdomen were respectively 51, 40.5 and 42 cm. His body temperature was 40 C. (104 F.). Physical and laboratory examinations revealed no cause for the hyperpyrexia, which persisted for five months. During this time the body temperature ranged from 37.8 to 40 C. (100 to 104 F.), occasionally falling to 37.2 C. (99 F.) or rising to more than 40.5 C. (104.9 F.). Aside from lassitude and some cerebral deterioration, no gross neurologic abnormality was found. The eyegrounds were normal, and vision was good; the tendon reflexes were slightly hyperactive, and sensation was grossly normal. The leukocyte count was 11,000, the erythrocyte count

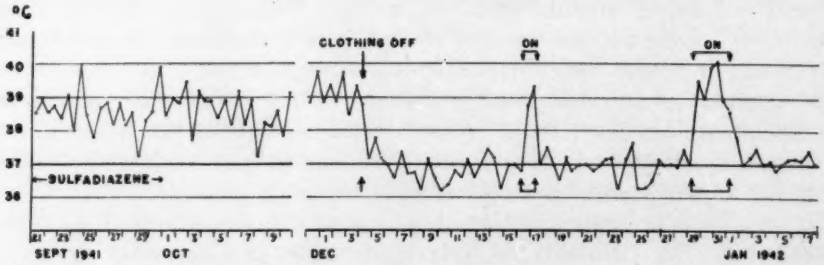

Chart 1.—Curves of the patient's daily rectal temperature. The portion at the left of the break is typical of his temperature range for five months; the portion on the right represents the effect of undressing and dressing the patient.

5,600,000 and the hemoglobin content 95 per cent. Chemical studies of the blood revealed: calcium, 11.1 mg. per hundred cubic centimeters, and phosphorus, 4.8 mg.; sodium, 140 milliequivalents, and chlorine, 103 milliequivalents, per liter; cholesterol, 94 mg. per hundred cubic centimeters. Repeated cultures of blood and of urine gave negative results. Results of tests for agglutination and of examinations of the spinal fluid were normal. Sulfadiazine and acetylsalicylic acid failed to affected the hyperthermia. Weight and height remained essentially constant in spite of a poor appetite and little activity.

On December 2, the patient's clothing, except for a diaper, was removed, and the room temperature was regulated between 20 and 22 C. (68 and 72 F.). Within six hours his body temperature fell to normal and remained there for one week. His clothing was then replaced for twenty-four hours, and his rectal temperature rose to 39 C. (102 F.). With removal of clothing his temperature again fell to normal. This period of dressing was repeated one and two weeks later, with the same results. On the latter occasion he was given 1½ grains (0.1 Gm.) of phenobarbital, without effect on his temperature (chart 1). Each time the body temperature was high, the patient was flushed, irritable and restless. Sweating was noticeable on the head, hands and feet, but not on the trunk.

From Dec. 2, 1941 to April 2, 1942, the patient's temperature was kept at approximately 37 C. (98.6 F.) by exposing the skin and controlling the surrounding temperature. With the disappearance of the hyperthermia the patient began slowly to improve in appetite and activity, and at the time of discharge from the hospital he weighed 8,150 Gm. (17 pounds 15 ounces), could roll over in his crib, though he could not sit up or stand, and was again using a few words.

Because the patient presented the picture of poikilothermia, a series of measurements of his heat production under various conditions of body temperature were carried out. The

routine method in practice at the Massachusets General Hospital for measuring respiratory metabolism of infants [2] was used throughout this study. It consists of measuring the carbon dioxide production in a respiration chamber with constant ventilation. The method is accurate to ± 5 per cent. Body temperature was measured by a rectal thermocouple. All observations were made with the child in the resting state. The values for heat production are reported as calories per twenty-four hours.

During the time that measurements were being made, the patient was on a fixed diet of 817 calories daily, derived from 72 Gm. of carbohydrate, 41 Gm. of fat and 40 Gm. of protein. He was kept in an environment which maintained his body temperature close to normal.

Three series of measurements of heat production were made. In the first series the body temperature was stationary at five different levels; in the second, body temperature was rising; in the third, it was falling.

RESULTS

The data obtained in all tests are recorded in the table.

In the first series of five observations, it will be seen that the heat production was essentially the same each time, without regard to the rectal temperature level.

Heat Production Under Various Conditions of Body Temperature

Series	I					II			III			
Test	1	2	3	4	5	6	7	8	9	10	11	12
Date, 1942	1/9	1/14	1/20	1/22	2/18	1/27	2/3	2/16	2/24	2/26	3/3	3/9
Total time in chamber, minutes	50	49	57	63	68	94	90	65	71	90	90	72
Air temperature in chamber, average	21.5	24.0	24.6	22.1	24.1	23.0	22.8	24.9	20.8	23.3	23.0	23.0
Wall temperature of chamber	23.5	25.0	25.2	23.8	25.2	23.9	23.0	25.4	7.6	8.2	9.4	9.8
Average rectal temperature for week before test	37.3	37.7	37.5	37.2	37.7	37.5	37.0	37.7	37.0	36.9	36.9	37.2
Rectal temperature, C.												
Initial	34.8	38.9	39.8	38.5	37.6	38.1	36.1	37.5	38.0	37.0	37.6	37.6
Final	35.1	39.1	39.9	38.5	37.6	39.2	37.3	38.9	35.4	34.7	34.6	35.5
Total change	+0.3	+0.2	+0.1	±0	±0	+1.1	+1.2	+1.4	—2.6	—2.3	—3.0	—2.1
Average total calories per 24 hours	574	593	572	596	628	663	648	653	490	500	456	440
Normal total calories per 24 hours for weight	453	434	434	443	441	443	426	441	444	445	438	445
Normal total calories per 24 hours for height	400	400	400	400	404	400	404	404	404	404	408	416
Average basal metabolic rate for weight and height	+36	+42	+37	+42	+49	+58	+56	+55	+16	+18	+8	+2

Arranged in order of ascending temperature, the twenty-four hour values for heat production were:

34.8 C.	574 calories
37.6 C.	628 calories
38.5 C.	596 calories
38.9 C.	593 calories
39.8 C.	572 calories

These values all fall within 6 per cent of the mean, 593 calories. The greatest change in temperature during any of the measurements in this series was 0.3 degrees (C.) in fifty minutes. Except for the abnormal temperatures, these measurements were comparable to those obtained in the usual metabolism test. Compared with the normal standards for weight and height at the patient's age, his basal metabolic rate was + 42 per cent. This high value was probably due to his

2. Higgins, H. L., and MacLaren, W. R.: Simpler Methods for Determining Basal Metabolic Rates of Children, Am. J. Dis. Child. **58**:670-671 (Sept.) 1939.

short compact stature. The ease with which hyperthermia developed when the patient was wearing light clothing may be attributed, in part, to his greater than normal need for loss of heat.

In the second series of measurements, the child's temperature was raised by wrapping him in a light blanket at the time he was placed in the metabolism chamber. The rise began at once and continued throughout each test. The collection of samples of carbon dioxide was not begun until the child had been in the chamber for thirty minutes to an hour. The average heat production was 655 calories, as compared with 593 calories when the child's temperature was constant. This was an average increase of 11 per cent in heat production for temperature increases of 0.8, 0.8, and 1 degree (C.). No flushing of the skin was noted, and sweating was apparent only at the end of test 6, when the patient's temperature was 39.2 (102.6 F.).

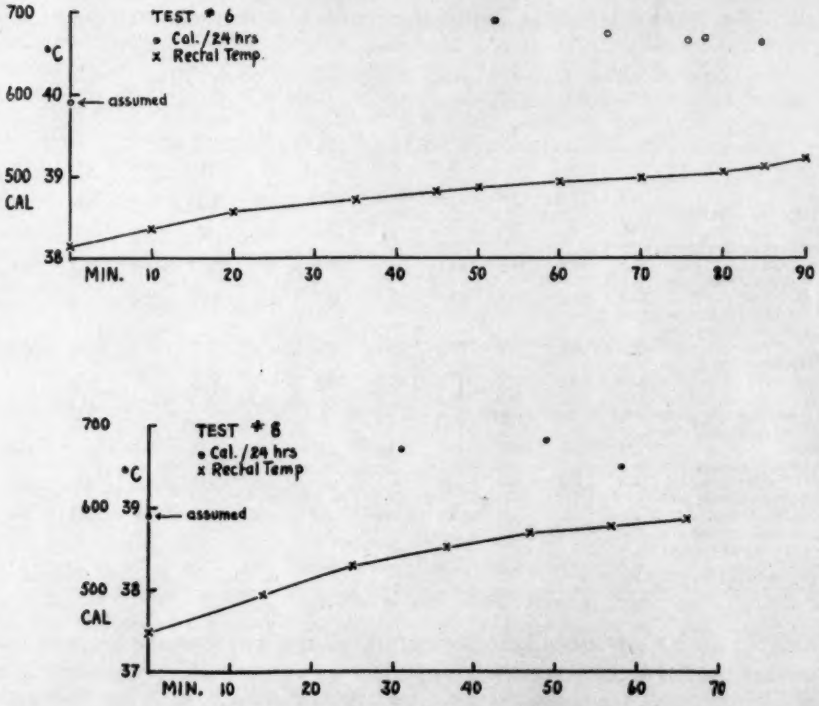

Chart 2.—Response of body temperature and heat production to wrapping patient in a blanket in tests 6 and 8. Time is counted from application of the blanket.

The third series of measurements, in which cold water was run into the water jacket of the metabolism chamber after the child had become quiet, was characterized by a pronounced fall in body temperature and lowered heat production. The decline in temperature began as soon as cooling was started and ranged from 2.1 to 3 degrees (C.) in seventy to ninety minutes. The average heat production measured toward the end of the cooling period was 472 calories. This represents a decline from his normal resting value (593 calories) of 21 per cent. No shivering, muscle tonus or restlessness was observed, although the rectal temperature fell well below normal in each test.

Representative curves of heat production and change in temperature in series II and III are shown in charts 2 and 3.

COMMENT

This patient's heat production varied from the normal in three respects. The first was the constant heat production without reference to the body temperature over the range 34 to 39 C. (93 to 102 F.), provided that the temperature had been stationary for some time. The second was the increase in heat production with rising body temperature. Ordinarily, when loss of heat from the body is impeded, heat production remains constant or declines slightly, and vasodilatation and sweating come into play before any rise in body temperature is apparent.[3] The third respect was the concomitant fall in body temperature and heat production without attempts at counteraction. The normal person in a cold environment will

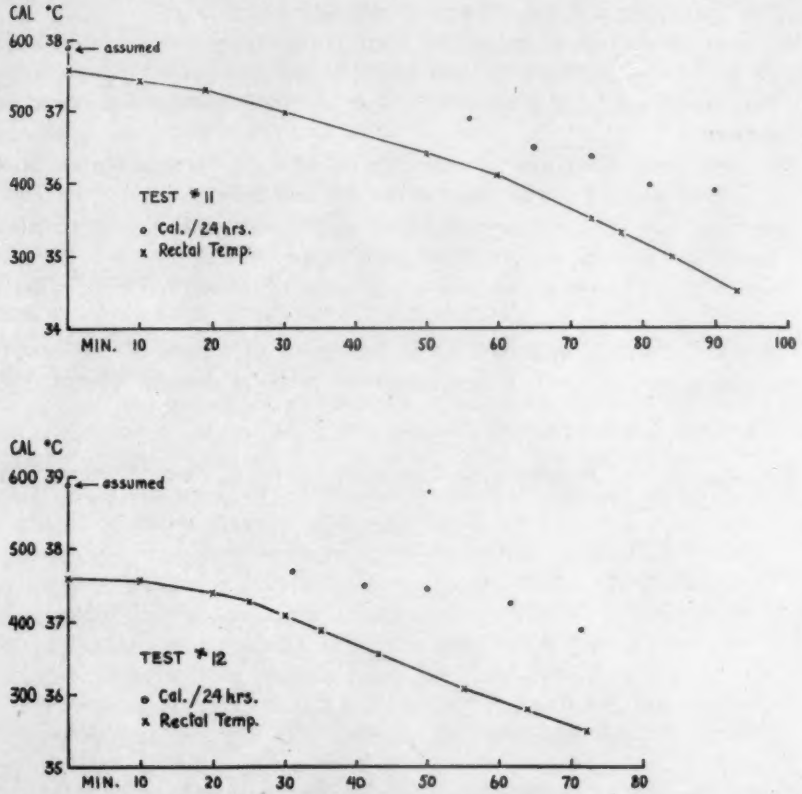

Chart 3.—Response of the patient's temperature and heat production to cooling in tests 11 and 12. Time is calculated from the point of introducing cold water into the calorimeter. The assumed average initial value of heat production of 593 calories per twenty-four hours is indicated in charts 2 and 3.

increase his heat production twofold or threefold if necessary to combat a fall in body temperature.[4]

The behavoir of this patient is strongly suggestive of that of a "cold-blooded animal" and is presumably due to the failure of the heat-regulating center. On

3. Hardy, J. D., and Soderstrom, G. F.: Heat Loss from the Nude Body, and Peripheral Blood Flow at Temperatures of 22° to 35° C., J. Nutrition **16**:493-590 (Nov.) 1938.

4. Dill, D. B., and Forbes, W. H.: Respiratory and Metabolic Effects of Hypothermia, Am. J. Physiol. **132**:685-697 (April) 1941.

the evidence derived by Ranson from monkeys,[5] the area involved probably includes the caudal portion of the hypothalamus. Destruction here is said to lead to complete poikilothermia, with absence of shivering at low temperatures and of vasodilation and sweating at high. In our patient such a lesion would be only a part of a widespread acquired cerebral damage, which became apparent two months before he was admitted to the hospital. An encephalitis of unknown origin seems to have been a probable cause for this picture.

SUMMARY

The case of a 3 year old achondroplastic dwarf with poikilothermia is presented.

His body temperature could be varied almost at will by adjusting the environmental temperature and the amount of clothing worn.

His heat production at stationary body temperature was constant over as wide a range as 34.8 and 39.8 C. (94.6 and 103.7 F.).

When heat loss was excessive, the body temperature and heat production fell together.

The child was relatively comfortable at all body temperatures up to 39 C. (102.2 F.), at which level he became restless and uneasy.

Sweating was absent over the trunk, and vasodilatation and sweating on the head, hands and feet appeared only at high temperatures.

Shivering and increased muscle tonus were not observed even when the body temperature fell as low as 34.6 C. (94.3 F.).

The poikilothermia appeared to be the result of failure of the heat-regulating center, which was involved in a widespread cerebral damage of unknown causes.

300 Longwood Avenue, Boston.

5. Ranson, S. W.: Regulation of Body Temperature, A. Research Nerv. & Ment. Dis., Proc. (1939) **20**:342-399, 1940.

HEMOLYTIC STREPTOCOCCUS MENINGITIS IN INFANTS UNDER THREE MONTHS OF AGE

A REVIEW OF THE LITERATURE AND A REPORT OF A CASE WITH RECOVERY

HARRY GIBEL, M.D.
AND
ABRAHAM M. LITVAK, M.D.
BROOKLYN

Hemolytic streptococcus meningitis in infants under 3 months of age is rare. A careful review of the literature yielded 56 reported cases with only 2 recoveries. We are adding a third case with recovery.

Meningitis in infants under 3 months of age is not unusual. Reports during the last forty-seven years include meningitis caused by almost every organism known. In a review of the literature it is noted that some types of infection occur more frequently than others, and in infants under 3 months of age the order of frequency of causative organisms is as follows: Bacillus coli, Pneumococcus, Meningococcus, hemolytic streptococci, Streptococcus viridans, Staphylococcus aureas, Bacillus pyocyaneus, Bacillus lactis aerogenes, Bacillus mucosus capsulatus and Bacillus influenzae.

In 1937, before the use of the sulfonamide compounds for treatment of streptococcic meningitis, one of us (A. M. L.) [1] summarized the literature on this disease and collected 123 cases of recovery from it. The patients were of all ages; the youngest was 21 months old. With the introduction of the sulfonamide drugs in the treatment of streptococcic meningitis numerous cases of recovery of older children and adults have been recorded in the literature. The fatality rate of this disease has been reduced from nearly 100 to 15 per cent. Cases of recovery are no longer recorded in the literature. The introduction of sulfanilamide and its derivatives in the treatment of streptococcic meningitis has altered the attitude toward this disease heretofore regarded as almost universally fatal. On the other hand, for very young infants, because of the notorious delay in establishing the diagnosis of meningitis, the mortality rate has not been significantly reduced.

REVIEW OF THE LITERATURE

The first cases of meningitis in infants under 3 months of age were reported in 1895 by Scherer,[2] who recorded 3 cases of B. coli meningitis.

Holt [3] in 1911 reported 300 cases of meningitis in infants and children. Of these, 197 had been observed since the introduction of the lumbar puncture for diagnosis and treatment. In 10 of these the disease was due to a staphylococcic or streptococcic infection, and in only 6 was the patient a newborn infant. In 2

From the Pediatric Department of the Brooklyn Jewish Hospital, Dr. Benjamin Kramer, Pediatrician in Chief.

1. Litvak, A. M., and Klughertz, M. B.: Otogenic Streptococcic Meningitis: Review of Recent Literature with Report of Recovered Case, Arch. Pediat. **54**:714 (Dec.) 1937.

2. Scherer, F.: Ein Beitrag zur Aetiologie der Leptomeningitis purulenta bei Säuglingen, Jahrb. f. Kinderh. **39**:1 (Jan.) 1895.

3. Holt, E. L.: Observations on Three Hundred Cases of Acute Meningitis in Infants and Young Children, Am. J. Dis. Child. **1**:26 (Jan.) 1911.

of the cases meningitis occurred as a primary infection; in 5 the infection was secondary to spina bifida, and in 1 it followed an operation for hydrocephalus.

In 1916 Koplik [4] reported 12 cases of meningitis in infants under 3 months which he had observed during the years 1909 to 1915. In 4 of these the disease was caused by meningococci; in 1 by colon bacilli; in 3, by pneumococci, and in 4 by streptococci. Two of the children with streptococcic meningitis were 6 weeks old; 1 was 7 weeks old, and 1 was 3 months old.

Barron [5] in 1918 collected 39 cases of meningitis in infants under 3 months of age. His report does not include any cases of streptococcic meningitis.

In 1921 Neal [6] and her associates, of the Meningitis Division of the New York Department of Health, reported 692 cases of meningitis observed by them in the preceding ten years. In 49 of these the infection was due to streptococci. Unfortunately, no ages were given.

Cooke and Bell [7] reported 2 cases of staphylococcic and streptococcic meningitis observed at the St. Louis Children's Hospital. In 1 case the disease occurred in

Summary of Cases of Streptococcic Meningitis in Infants Under 3 Months of Age

Year	Author	Cases	Recoveries
1911	Holt [3]	6	0
1916	Koplik [4]	4	0
1922	Cooke and Bell [7]	2	0
1926	Neal [8]	12	0
1927	McGee [9]	1	0
1928	Smith [10]	1	0
1929	Köhler [11]	1	0
1930	Guéniot [12]	1	0
1930	Cruickshank [13]	7	0
1933	Fothergill and Sweet [14]	9	0
1935	Ravid [15]	2	0
1936	Craig [16]	4	0
1942	Levinson [20]	4	0
1942	Appelbaum [21]	2	2
1942	Gibel and Litvak	1	1
	Total	57	3

a 22 day old infant who had a spina bifida. In the second it occurred in a 2 month old child with an abscess of the brain.

Another report by Neal,[8] in 1926, analyzed 1,500 cases of meningitis. In 50 of these the patients were infants up to 3 months of age; in 11 of the 50 the infection was of streptococcic origin, and in 1 it was a combined infection caused by hemolytic streptococci and Staphylococcus albus.

McGee [9] reported a case of meningitis in a 2 week old infant; the etiologic organism, however, was not definitely ascertained. The organisms isolated at the

4. Koplik, H.: Meningitis in the New-Born and in Infants Under Three Months of Age, Arch. Pediat. **33**:481 (July) 1916.

5. Barron, M.: Meningitis in the Newborn and in Early Infancy, Am. J. M. Sc. **156**:358 (Sept.) 1918.

6. Neal, J. B.: Influenzal Meningitis, Arch. Pediat. **38**:1 (Jan.) 1921.

7. Cooke, J. V., and Bell, H. H.: The Incidence of Meningitis in Early Infancy, with a Description of Two Cases Due to Unusual Organisms, Am. J. Dis. Child. **24**:387 (Nov.) 1922.

8. Neal, J. B.: Meningitis Caused by Bacilli of the Colon Group, Am. J. M. Sc. **172**:740 (Nov.) 1926.

9. McGee, W. A.: Meningitis of Mixed Type in a Two Weeks Old Infant, Arch. Pediat. **44**:636 (Oct.) 1927.

first lumbar puncture were thought to be meningococci, while fluid obtained at the second lumbar puncture yielded hemolytic streptococci.

Smith [10] reported a case of hemolytic streptococcus meningitis in a 5 day old infant, and Köhler [11] reported a case of the same infection in a 2 day old infant. A report shortly followed in which Guéniot [12] recorded a similar infection in a 16 day old infant.

Cruickshank [13] reviewed 800 cases of neonatal death at the Glasgow Royal Maternity and Women's Hospital. He found meningitis as the cause of death in 33 cases, or 4 per cent. The ages of the infants who died varied from 2 to 17 days, while 88 per cent of the deaths took place during the period from the fifth to the thirteenth day. Nineteen of these children were mature, and 14 were premature. There was evidence of generalized septicemia in 29 cases. Pneumonia was encountered in 12 cases, and in the others such conditions as peritonitis, pleurisy and pericarditis were found. In 10 cases no satisfactory bacteriologic results were obtained. In the remaining 23 cases the following organisms were found: B. coli in 11; streptococci in 7, and B. pyocyaneus in 1. In some of the cases of streptococcic infection coliform organisms were present in addition.

In 1933 Fothergill and Sweet [14] reviewed 705 cases of meningitis from the Infants and Children's Hospitals of Boston from 1921 to 1933. In 69 of these the meningitis was due to hemolytic streptococci, and only 9 of the patients were 3 weeks old or less (3 were 3 weeks old; 3 were 2 weeks old, and 3 were 1 week old).

Ravid [15] reported 2 cases: In 1 an 18 day old infant had hemolytic streptococcus meningitis, and in the other a 4 week old infant had a combined coli and streptococcic infection.

Craig [16] reported 21 cases of meningitis and included in this series 3 cases in which the disease was due to Str. viridans and 1 in which it was due to a combination of hemolytic streptococci, Staph. aureus and B. coli. The 4 patients died within the first three weeks of life.

The first case of streptococcic meningitis in an infant who recovered was recorded by Basman and Perley.[17] Their patient was a 20 month old infant and was the first of such an age to recover at the St. Louis Children's Hospital. This recovery took place after the introduction of the sulfonamide compounds in the treatment of this disease, and sulfanilamide was the drug used in the treatment. This report was followed by a report of a case by Cardelle,[18] who recorded the recovery of a 6 month old infant.

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10. Smith, L. H.: Streptococcus Meningitis: Report of a Case in a Five Day Old Infant, Northwest Med. **27**:345 (July) 1928.
11. Köhler, N.: Hirnhautentzündung beim Neugeborenen, Zentralbl. f. Gynäk. **55**:2291 (Jan.) 1929.
12. Guéniot, P.: Méningite streptococcique foudroyante survenue le 16e jour après la naissance, Nourrisson **18**:304 (Sept.) 1930.
13. Cruickshank, J. N.: Child Life Investigations: The Causes of Neonatal Death, Medical Research Council, Special Report Series, no. 145, London, His Majesty's Stationery Office, 1930.
14. Fothergill, L. D., and Sweet, L. K.: Meningitis in Infants and Children with Special Reference to Age Incidence and Bacteriologic Diagnosis, J. Pediat. **2**:696 (June) 1933.
15. Ravid, J. M.: Meningococcic and Nonmeningococcic Meningitis in Newborn and in Young Infants, Am. J. Dis. Child. **49**:1282 (May) 1935.
16. Craig, W. S.: Meningitis in Newborn, Arch. Dis. Childhood **11**:171 (Aug.) 1936.
17. Basman, J., and Perley, A. M.: Report of Patients Treated with Sulfanilamide at St. Louis Children's Hospital, J. Pediat. **11**:212 (Aug.) 1937.
18. Cardelle, P. G.: Meningitis estreptocóccica en un lactante. Tratamiento por sulfanilamida (método de Retan). Curación, Arch. Soc. estud. clín. Habana **33**:257 (May) 1939.

In 1938 Neal [19] and her associates again reviewed the records of the meningitis division of the Department of Health of the City of New York and reported on a total of 3,502 cases of meningitis. In this group of cases, 92 patients were infants under 3 months of age, and in 14 of these the disease was caused by streptococci. Figures for mortality were not given, but it is our impression that all patients in the 3 month age group died. This report added cases of 2 patients in that age group who were not included in her previous report.

Levinson [20] recorded 4 cases of meningitis in infants under 3 months. Three of these, a 3 day old infant, one of 6 weeks, and one of 7 weeks, were reported as having hemolytic streptococcus meningitis, and he added 1 case of Str. viridans meningitis in an 8 day old infant.

Dr. Emanuel Appelbaum,[21] director of the meningitis division of the New York Department of Health, who has had a most extensive experience with meningitis, stated in a personal communication to us that he had had only 2 recoveries from hemolytic streptococcus meningitis in infants. One baby was 13 days old; the second was 1 day old. The first was treated with sulfapyridine and azosulfamide (disodium 4-sulfamidophenyl-2′-azo-7′-acetylamino-1′-hydroxynaphthalene-3′,6′-disulfonate); the second was treated with sulfadiazine.

In a careful review of the literature we have, therefore, found reports of 56 cases of streptococcic meningitis in infants under 3 months of age. These cases were reported over a period of forty-seven years (from 1895 to 1942). In all these cases, only 2 recoveries are reported. We are adding a third.

REPORT OF CASE

S. D., a boy aged 21 days, was admitted to the Brooklyn Jewish Hospital on Jan. 6, 1942. The complaint on admission was difficulty in arousing the baby for the preceding twelve hours.

The baby was born at term; the pregnancy was normal; labor was uncomplicated, and delivery was spontaneous. There was no postnatal cyanosis or convulsions. The birth weight was 6 pounds and 8 ounces (2,948 Gm.). Ever since his discharge from the hospital the infant had appeared irritable and had cried a good deal, especially at night. The morning before admission for this illness he did not awaken for his bottle, whimpered in his sleep and could not be aroused.

Feedings were forced all day, and toward evening the mother noted some cyanosis. During all this time there had been no coughing, vomiting, fever or convulsions. When seen before admission by one of us (A. M. L.), the baby was in collapse.

On admission the baby was in shock and his rectal temperature was 97 F. He was cold and cyanotic, and the skin had a bluish mottling. Respirations were shallow and gasping, and a response could not be elicited to painful stimuli. Occasionally respirations would stop completely, and breathing had to be stimulated by compression of the chest.

The anterior fontanel was tense and bulging, but there was no nuchal rigidity. Both ear drums and the mucous membranes of the nose and throat were normal. The pupils reacted to light, and nystagmus was not present. The heart and lungs were normal to percussion and auscultation. The abdomen was soft throughout, and only the tip of the liver was palpable. There was no hypertonicity of the extremities. All deep reflexes were hyperactive; the abdominal reflexes were absent.

On the patient's admission the hemoglobin content was 90 per cent; the red cell count was 4,600,000 and the white cell count 10,200, with 75 per cent polymorphonuclears and 25 per cent lymphocytes. Spinal tap in three different interspaces produced bloody spinal fluid.

The patient was placed in an oxygen tent and given sulfadiazine, 1 grain (0.06 Gm.) every four hours. Because of his inability to swallow, medication and feedings were given by gavage.

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19. Neal, J. B.: The Treatment of Acute Infection of the Central Nervous System with Sulfanilamide, J. A. M. A. **111**:1353 (Oct. 8) 1938.

20. Levinson, A., in Brennemann, J.: Practice of Pediatrics, Hagerstown, Md., W. F. Prior Company, 1942, vol. 4, chap. 8.

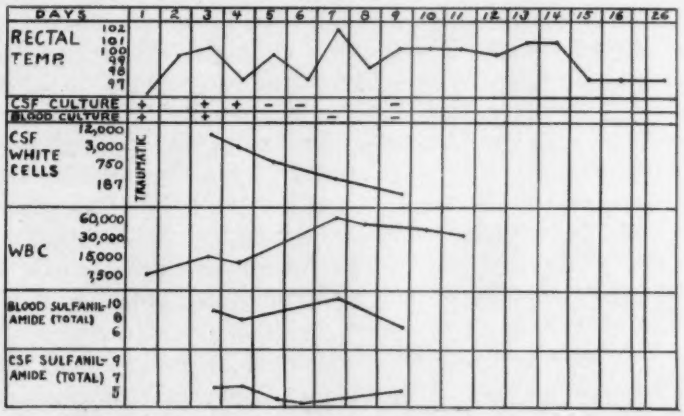
21. Appelbaum, E.: Personal communication to the authors.

A continuous intravenous injection of 5 per cent dextrose in physiologic solution of sodium chloride was started to overcome shock and dehydration.

Course of the Disease (chart).—The next morning (January 7) respirations were 80 per minute and very shallow. The eyes showed a tendency to roll upward. The skin, however, was warmer and the color better. Thirty hours after admission, the spinal fluid was reported to contain hemolytic streptococci. At that time medication was changed to sulfanilamide, 2 grains (0.13 Gm.) every four hours.

On January 8, the child's third day in the hospital, the fontanel again became full and tense and generalized muscular spasticity was noted. A second spinal tap was performed to reduce the intracranial pressure. The fluid was cloudy and contained 12,500 cells, all of which were atypical or degenerated polymorphonuclear cells. The spinal fluid contained 25 mg. of sugar and 385 mg. of protein per hundred cubic centimeters, and the culture again yielded hemolytic streptococci. On this day culture of the blood was also reported to show hemolytic streptococci. The dose of sulfanilamide was increased to 3 grains (0.19 Gm.) per pound (0.5 Kg.) of body weight per twenty-four hours.

On the fourth day in the hospital the child was still stuporous and would not swallow. Opisthotonos and nuchal rigidity appeared and rapidly became severe. Lumbar puncture was again performed. The spinal fluid now contained 3,760 cells, all polymorphonuclear cells, and 33 mg. of sugar and 297 mg. of protein per hundred cubic centimeters. The chloride content was 443 mg. per hundred cubic centimeters. Culture still yielded hemolytic streptococci. The



Clinical course of a 3 week old infant with hemolytic streptococcus meningitis.

level of sulfanilamide in the spinal fluid was 6.9 mg. per hundred cubic centimeters (total) and in the blood 8.5 mg. (total).

On the patient's fifth day in the hospital the opisthotonos and nuchal rigidity were less pronounced. The spinal fluid contained 1,130 cells, all polymorphonuclear cells; the fluid was sterile on culture, and organisms were not seen on smears.

On the sixth day the fontanel was bulging again. The fluid was still sterile, but the level of the drug was only 4.5 mg. per hundred cubic centimeters. A hypodermoclysis containing 15 grains (0.97 Gm.) of sulfanilamide was given. Thereafter the blood level of the drug rose to 13.5 mg. per cent (total).

On the seventh day the opisthotonos began to subside. On the ninth day the last lumbar puncture was performed. The spinal fluid at this time was clear, contained 240 cells and a normal amount of sugar and was sterile on culture; organisms were not found on smears. The first sterile blood was obtained on this day.

Chemotherapy was continued for twenty-three days. By the eighth day in the hospital improvement was noted, and from then on the clinical course was satisfactory. There was a steady gain in weight; the cranial sutures did not separate, and the head did not increase in size. The source of the infection could not be determined. Cultures of materials from the nose and throat never contained hemolytic streptococci. The mucous membranes of the nose and throat were always normal. The ear drums at all times presented a normal appearance. The umbilicus was healed and dry. Stools and urine did not contain the hemolytic streptococci.

At the time of writing, ten months after the patient was discharged from the hospital, he is growing normally. He weighs 20 pounds (9.1 Kg.) and is 30 inches (76 cm.) long. The size of his head is normal for his age. Mentally and physically he appears normal, and on neurologic examination no abnormalities are noted.

SUMMARY

Hemolytic streptococcus meningitis in an infant under 3 months of age is relatively unusual. Fifty-six cases were reported from 1895 to 1942; in only 3 is recovery known to have occurred. A review of the literature is presented and the case of a 21 day old infant who recovered is reported.

1145 Eastern Parkway.

PANCREATIC ENCEPHALOPATHY

REVIEW OF THE LITERATURE, WITH REPORT OF A CASE

LOUIS A. LURIE, M.D.
AND
SOL LEVY, M.D.
CINCINNATI

The occurrence of psychoses in children was formerly considered to be rare. This has been disproved by more recent investigations.[1] Even today most physicians when dealing with psychoses in children and adolescents usually think only in terms of the affective psychoses, such as schizophrenia. However, many psychotic episodes which occur in children are definitely of the nature of toxic psychoses. Very often these occur during or following the course of an acute infectious disease, such as measles or pertussis. As a result, the basis for the psychotic manifestations was thought to be an associated encephalitis.

However, more recent pathologic investigations have shown that these episodes are not necessarily the result of an inflammatory process in the brain but may be due to degenerative cerebral changes. Hence, instead of "the encephalitides," the term "encephalopathy" was introduced. Jochims,[2] in 1928, first used the term "pertussis encephalopathy" to describe the degenerative changes in the brain which occurred during an attack of whooping cough and which were responsible for the definite neurologic and mental changes noted in the patients. Recently this conception has been substantiated clinically by the investigation of Lurie and Levy.[3] Following Jochims' study, encephalopathies were described as occurring during the course of many other diseases, but principally in association with acute infectious diseases, such as measles, chickenpox and whooping cough.

Later investigations, however, have shown that an encephalopathy may occur during or following the attack of any somatic disease or intoxication. Bender and Schilder [4] in 1933 described an "encephalopathia alcoholica" and Wechsler [5] in discussing this paper stated that in his opinion alcoholic and other neuritides are toxic degenerative states on the basis of avitaminosis. His conception was corroborated by Jolliffe,[6] who in 1940 described a so-called "nicotinic acid deficiency encephalopathy." He reported that even in far advanced stages of so-called alcoholic encephalitis the patient can be cured in many instances by appropriate therapy with nicotinic acid and expressed the opinion that this disease is essentially a vitamin deficiency.

From the Child Guidance Home of the Jewish Hospital.

1. Lurie, L. A.; Tietz, E. B., and Hertzman, J.: Functional Psychoses in Children, Am. J. Psychiat. **92**:1169, 1936.

2. Jochims, J.: Ein Beitrag zur Keuchhusten-Encephalopathie, Ztschr. f. Kinderh. **45**: 326, 1928.

3. Lurie, L. A., and Levy, S.: Personality Changes and Behavior Disorders of Children Following Pertussis, J. A. M. A. **120**:890 (Nov. 21) 1942.

4. Bender, L., and Schilder, P.: Encephalopathia alcoholica, Arch. Neurol. & Psychiat. **29**:990 (May) 1933.

5. Wechsler, I. S., in discussion on Bender and Schilder.[4]

6. Jolliffe, N.; Bowman, K. M.; Rosenblum, L. A., and Fein, H. D.: Nicotinic Acid Deficiency Encephalopathy, J. A. M. A. **114**:307 (Jan. 27) 1940.

More recently attention has been focused on the possible role of organic somatic disease in the production of encephalopathies with resultant mental symptoms. This has been especially noteworthy in the case of pancreatic disease.

The first observation of this nature was reported by Lovell,[7] who observed definite pathologic changes in the pancreas in patients suffering from involutional melancholia. Drury and Farran-Ridge [8] observed a similar anxiety syndrome in patients dying from acute pancreatitis. Practically all the reports attributed the mental symptoms occurring during the course of pancreatic disease to a state of hyperinsulinism. Recently, however, several reports have been published describing a definite clinical syndrome with mental, neurologic and pathologic symptoms which occur in association with organic pancreatic disease and which are in no way similar to the mental symptoms which have been reported as occurring during the state of hyperinsulinism. The clinical picture in the former is that of an acute toxic psychosis, while in the latter the mental picture is more of the type of an exhaustion psychosis. The anatomic-pathologic picture as far as the pancreas and the brain are concerned is also entirely different in the two conditions.

In a recent paper on "pancreatic encephalopathy" Rothermich and von Haam [9] reported 8 cases in which "the syndrome bears sufficient characteristic features from the psychiatric as well as the neurologic point of view to lend itself to the proper differential diagnosis." The clinical picture in these cases, as far as the mental symptoms were concerned, was characterized by a rather abrupt onset with confusion and marked agitation. In some cases there were auditory and visual hallucinations and delusions of persecution. A pronounced speech defect of a slurring type was present in almost all the patients. In addition, the speech was both incoherent and irrelevant. There were often complete disorientation and total lack of insight and judgment. This state occasionally was interrupted by lucid intervals, during which the patients conversed fairly rationally and intelligently. However, these rational intervals were of short duration. Rothermich and von Haam found neurologic symptoms which they considered characteristic in all of their patients. The outstanding symptom was a pronounced spasticity of the muscles of the extremities and of the neck, which was of the waxy or cogwheel type and which gave rise to pain if any group of muscles was extended. The deep tendon reflexes were hyperactive but equal. The abdominal reflexes were absent, and occasionally there was a clonus or a positive reversal of the plantar reflexes. A strong grasping reflex, which manifested itself in the later stages of the disease, was also noted.

Another characteristic of the disease was that it showed a strong tendency to spontaneous recovery. All the mental symptoms disappeared, and the patients made a complete recovery in a comparatively short space of time. The exception to this occurred in those cases in which the pancreatic involvement was so severe that death resulted.

Rothermich and von Haam stressed the importance of the medical history. In all the cases the history revealed recurrent attacks of gastric distress or pains in the stomach which had been present either for many years before any mental changes were noted or had occurred just shortly before the onset of the psychosis.

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7. Lovell, C.: Cerebral Oedema in Certain Mental Disorders, Brit. M. J. **2**:656, 1937.

8. Drury, K. K., and Farran-Ridge, C.: Some Observations on the Types of Blood-Sugar Curve Found in Different Forms of Insanity, J. Ment. Sc. **71**:8, 1925.

9. Rothermich, N. O., and von Haam, E.: Pancreatic Encephalopathy, J. Clin. Endocrinol. **1**:872, 1941.

Most patients complained of pains in the abdomen, loss of appetite and nausea and vomiting. Very often these symptoms were so severe that the patients refused to eat or drink.

In order to confirm their clinical diagnosis, they performed various laboratory tests, such as the determination of the diastase levels of the blood and urine. However, these tests have their limitations, because the diastase remains elevated both in the blood and in the urine for only a short time. If the patients are not seen at the immediate onset of the disease, these laboratory tests are valueless.

Further confirmation of their clinical diagnosis was obtained by Rothermich and von Haam as a result of the autopsy observations in 7 of their cases. The changes in the pancreas consisted of more or less sharply circumscribed areas of fatty or glandular necrosis and a marked periductal fibrosis with dilatation of the medium-sized and smaller ducts and epithelial proliferations with metaplasia. Severe interstitial fibrosis leading to atrophy of the glandular tissue was also present. The lesions in the brain consisted of small focal areas of capillary hemorrhage associated with perivascular edema and reactive gliosis. In some cases atrophy of the cortex was also present.

As to the cause of "pancreatic encephalopathy," the authors seemed inclined to agree with the hypothesis of Jolliffe and co-workers [6] of a "nicotinic acid deficiency encephalopathy," because "it could be easily possible that the pancreatic disease through its consequent frequent gastric upsets and disturbances of appetite precipitated a similar vitamin deficiency in our [Rothermich and von Haam's] patients. Such lack of proper nourishment over a period of time may well be sufficient to produce the acute nicotinic acid deficiency as described by Jolliffe." Rothermich and von Haam were further strengthened in this belief when they administered nicotinic acid to 1 of their patients and noticed a remarkable improvement in all of the symptoms within a short space of time.

These authors furthermore stated that "this syndrome of pancreatitis and encephalopathy is more common than one might at first consider."

The following case is in many respects similar to those reported by Rothermich and von Haam but is of especial interest because the patient was a young adolescent. The knowledge that a psychosis may occur in a child on the basis of an encephalopathy produced by a somatic disease is of extreme importance.

REPORT OF CASE

J. E., a white girl 14 years of age, was admitted to the Child Guidance Home because she suddenly began to manifest peculiar behavior reactions. She screamed uncontrollably, tossed her hands about, reached out for invisible objects and complained of smelling pepper and hearing cats miaowing. She also had many vague physical complaints and showed a pronounced loss of appetite and on occasion refused to eat. This change in her behavior became noticeable about three weeks prior to her admission to the Child Guidance Home. Up to that time the girl had never shown any evidence of peculiar or abnormal behavior reactions. The onset of this episode, which was abrupt, was characterized by extreme agitation, confusion and a near state of panic. She showed evidences of poor concentration and irrational thinking. She felt that she was being discriminated against in the schoolroom and that she was not getting credit for the work she was doing. She was undecided about what to wear and had great difficulty in making a decision. At times she was flighty and disoriented. There was extreme restlessness, and she did not sleep well at night. Most of the time she refused to eat.

The history showed that the patient, an only child, was born prematurely. Her infancy was not remarkable. Dentition was somewhat delayed; however, the girl walked and talked at the normal time. At the age of 6 years she suddenly suffered a severe asthmatic attack which was thought to be on an allergic basis. After this, the girl complained intermittently of pains in the stomach and of nausea and vomiting. Since that time, her appetite had been

only fair. At no time, however, did she present any peculiar behavior. She was always considered an emotionally stable child, and, as far as was learned, she was well adjusted both socially and academically.

The family history was entirely noncontributory. Both parents were in good health, and there was no history of epilepsy, mental or nervous disease, alcoholism, glandular disturbances, syphilis or any other type of hereditary or constitutional disease in any of the collaterals.

The physical examination showed a poorly developed and poorly nourished girl. She was 13½ pounds (6.1 Kg.) underweight for her height, which, in turn, was 2¼ inches (5.7 cm.) below the average. Except for considerable facial acne, the general physical examination disclosed normal conditions. However, the neurologic examination revealed the following facts: The facial muscles were rigid, and there was generally a blank expression. There was some indication of a grasping reflex; however, this was not pronounced. There was a fine tremor both of the outstretched hands and of the tongue. The deep tendon reflexes were hyperactive and equal, but the abdominal reflexes were absent. All the plantar reflexes were normal. The Romberg sign was slightly positive, and the gait was somewhat unsteady. There was some spasticity of the muscles of the extremities. Extension of these muscles produced pain. The spasticity was of the so-called waxy or cogwheel type.

From the endocrine standpoint, there was a strong suggestion of the presence of hypopituitarism of the Lorain-Levi type. Roentgenograms of the skull and of the sella turcica showed both to be normal.

Results of repeated blood counts and urinalyses were all within normal limits. The serologic reactions of the blood were negative. The tuberculin test also elicited a negative reaction. The basal metabolic rate was within normal limits. The blood chemistry showed normal values. No determination of the blood and urine diastase levels could be made because of the uncooperativeness of the patient. A dextrose tolerance test gave the following values: fasting blood sugar, 125 mg. per hundred cubic centimeters; one hour specimen, 178 mg.; two hour specimen, 135 mg., and three hour specimen, 68 mg. The corresponding specimens of urine all gave negative reactions for sugar and acetone.

Examination of the spinal fluid gave the following results: pressure, 150 to 200 mg.; cells, 1 lymphocyte per cubic millimeter; reaction for globulin, negative; Wassermann reaction, negative; gold curve, normal.

An electroencephalographic tracing was made, and the examiner reported as follows: "A six lead monopolar study was done. The record is good technically. There is a good 11 per second rhythm scattered throughout the record, much more prominent in the occipital leads. There is the usual amount of low voltage faster activity, which is for the most part normal beta rhythm. There are definitely scattered slow waves in all regions. These are between 5 and 6 per second; some of them have square tops and resemble the type of abnormality that has been described in psychomotor disorders and behavior problems. Hyperventilation does not slow the record noticeably. There is no evidence of localized abnormality and nothing to suggest an expanding lesion involving the cortex. Impression: This is a very mildly abnormal electroencephalogram, consistent with a mild cerebral dysrhythmia."

The girl's behavior during the period of observation at the Child Guidance Home was characterized by its pronounced unpredictability and abnormality. Most of the time she appeared to be in a state of panic, exhibiting extreme restlessness and fearfulness. At other times she was stubborn and negativistic. She refused to eat. Instead of sleeping at night, she wandered around the dormitories causing great disturbance. She expressed many fears regarding different objects in her bed which she claimed prevented her from sleeping. The girl washed her hands continually and most of the time ran around barefooted carrying her shoes and stockings in her hands. She seemed easily frightened by any noise. At such times, she shook all over and perspired excessively.

Often there was complete disorientation with total lack of insight and judgment. There was evidence of flight of ideas. Perseveration and stereotypy were noted. She expressed many ideas of persecution, and vivid auditory and visual hallucinations were elicited. Some of her actions were of the compulsive type. The emotional poverty was pronounced. A speech defect of the slurring type was present. Her gait was peculiar, the girl walking with short halting steps with the feet and legs held rigid while the body was bent forward. The face had almost a masklike appearance.

After five weeks her reactions gradually returned to normal, and when she was last seen (three months after discharge) she looked exceptionally well and no physical or mental abnormalities were detected. The neurologic symptoms were completely absent. According to the mother, the girl was getting along well both at home and in school and at no time

showed any evidences of her former abnormal behavior. The only treatment given in this case was a well balanced diet rich in vitamins.

COMMENT

The data from the history as well as from the clinical findings and the course of the disease are in accordance with Rothermich and von Haam's description of "pancreatic encephalopathy."

In this case the history revealed recurrent attacks of pains in the stomach and nausea and vomiting. This had been observed ever since the girl was 6 years old. Shortly before the onset of this disease, her eating habits became more erratic and most of the time she refused to eat. Rothermich and von Haam particularly stressed the importance of this symptom.

The outstanding neurologic findings were rigidity of the facial muscles with masklike expression, fine tremor of the tongue and hands, hyperactive deep tendon reflexes and absence of the abdominal reflexes. All the plantar reflexes were normal. There was spasticity of the muscles of the extremities, extension of which produced pain. The spasticity was of the so-called waxy or cogwheel type. There was some indication of a grasping reflex; this, however, was not pronounced. It was noteworthy that all the neurologic abnormalities disappeared on the subsidence of the psychosis.

The endocrine examination showed that the girl was considerably underheight and seriously underweight. The menarche had not yet commenced. These findings were suggestive of a Lorain-Levi type of pituitary dystrophy. This is noted because of the well known relationship between the pituitary gland and the pancreas.

Although no determinations of blood and urine diastase were made (owing to the patient's lack of cooperation), their absence is of no great significance; in all probability the results of such tests would have been negative, since the patient had been sick for at least three weeks before being admitted to the Child Guidance Home. According to Rothermich and von Haam, these tests are of no value at that stage of the disease.

We were unable to confirm Rothermich and von Haam's observation that during the onset of the acute attack there is a pronounced leukocytosis with increase in polymorphonuclear leukocytes. Repeated blood counts in this case revealed entirely normal findings. However, this might also be due to the fact, as has already been pointed out, that the patient was first observed three weeks after the onset of the attack. By that time the acute inflammatory processes in the pancreas may have already greatly subsided.

The roentgenograms as well as the electroencephalogram and other laboratory data did not reveal anything of specific value in regard to the diagnosis of this condition.

The psychotic picture was primarily that of an acute toxic psychosis. The onset of the disease was abrupt, with pronounced agitation and confusion. At times there was complete disorientation, and the patient lacked insight and judgment. The marked poverty of emotions was outstanding. Auditory and visual hallucinations as well as delusions of persecution were noted. A speech defect of the slurring type was present. Perseveration and stereotypy were also evident. Compulsive acts and attitudinizing were frequent. Lucid intervals appeared, during which the patient conversed fairly rationally and intelligently; however, these periods were infrequent and of short duration.

The patient made a spontaneous and sudden recovery. First the agitation and confusion subsided, and then the hallucinations as well as the delusions disappeared.

Repeated examinations since her recovery have failed to reveal anything abnormal either physically or mentally. Again, the complete disappearance of the neurologic symptoms should be noted.

SUMMARY AND CONCLUSIONS

A case of an acute toxic psychosis in a child with complete recovery is reported.

On the basis of the data derived from the personal history and from the physical, neurologic and psychiatric examinations as well as from the course of the disease, the diagnosis of pancreatic encephalopathy is made.

This is of importance, as it demonstrates that conditions other than acute infectious diseases may produce encephalopathies with resultant psychotic manifestations in children.

3149 Harvey Avenue.

Progress in Pediatrics

CONGENITAL ATRESIA OF PANCREATIC DUCT SYSTEM AS A CAUSE OF MECONIUM ILEUS

CRITICAL REVIEW OF THE LITERATURE, WITH A REPORT OF ONE CASE

WILLIAM KAUFMANN, M.D.
AND
DOROTHY B. CHAMBERLIN, M.D.
ALBANY, N. Y.

Meconium ileus, a rare condition found in newborn infants, was first described by Landsteiner [1] in 1905. At autopsy he found tough, inspissated meconium obstructing the ileum of a 5 day old child, together with occlusion of the major pancreatic duct and consequent pancreatic fibrosis. Since his original publication there have been other reports of this condition, most of them associated with severe lesions of the pancreas and its main ducts. A few cases without pancreatic changes have also been described, the major lesions being in the liver or in the intestine itself. The clinical symptoms in all cases are those of intestinal obstruction, and an accurate clinical diagnosis of the fundamental changes underlying the obstruction is usually impossible to make. Autopsy is necessary to disclose the nature of the lesion.

Recently an extremely interesting case of meconium ileus came to autopsy at the Albany Hospital, and it seems advisable to report it in some detail in the light of present knowledge of this condition.

REPORT OF A CASE

A white girl was born prematurely in the hospital on Nov. 13, 1941. The period of pregnancy had been normal, and there was no history of maternal syphilis. There was a low forceps delivery after a labor of twenty-three hours. The baby weighed 4 pounds 13 ounces (2,183 Gm.). She was placed in a heated crib and did well the first night. The following morning, however, it was noted that the infant vomited dark brown and green mucus and that the feedings were taken poorly. No meconium was passed, but a mucopurulent material drained from the rectum. The second day the abdomen became greatly ballooned, and distended loops of intestine were visible through the anterior abdominal wall. A colonic irrigation yielded only a small amount of mucus. A white semisolid stool was passed during the day. The infant refused to take her formula. That night vomiting became projectile and the abdominal distention became worse. The child's color was poor. A gavage tube was passed. Some flatus was expelled, and greenish mucus and curds were obtained. This procedure, however, did not relieve the distention. A barium sulfate enema filled the rectum, the sigmoid flexure and the distal half of the descending portion of the colon, but it was impossible to fill the remainder of the large intestine. Barium sulfate was introduced into the stomach through a tube. There was no definite dilatation of the stomach, and the barium passed immediately into the duodenum (fig. 1 *A*). Two hours later the barium had appeared in the upper loops of the jejunum. Just distal to this, with the patient in an inverted position, a loop of small intestine was visible. There were multiple fluid levels in the gas-distended

From the Department of Pathology and Bacteriology, Albany Medical College and the Laboratories of the Albany Hospital.

1. Landsteiner, K.: Darmverschluss durch eingedicktes Mekonium; Pankreatitis, Centralbl. f. allg. Path. u. path. Anat. **16**:903, 1905.

intestinal loops (fig. 1 *B*). A diagnosis of intestinal obstruction due to possible atresia of the lower part of the intestinal tract or due to compression from without was made, and a surgical consultation was held. Operation was decided on, and a transfusion of 75 cc. of citrated blood was given into the anterior fontanel. After this procedure the infant vomited and became cyanotic and, in spite of attempts at resuscitation died on November 16, sixty-eight hours after birth.

The essential pathologic changes noted at autopsy were limited to the gastrointestinal tract and the pancreas. The stomach and the first portion of the duodenum appeared normal for a newborn infant of this size and contained a moderate amount of barium. The remainder of the duodenum was slightly dilated, and a soft mixture of barium and intestinal contents was found in its lumen. The jejunum became progressively more dilated until two greatly distended loops were found in the proximal part of the ileum. These loops were filled with thick, mucoid, sticky, dark green meconium which could be forced out of the lumen only by continued firm pressure. In consistency it was like putty. The enlarged portion of the ileum

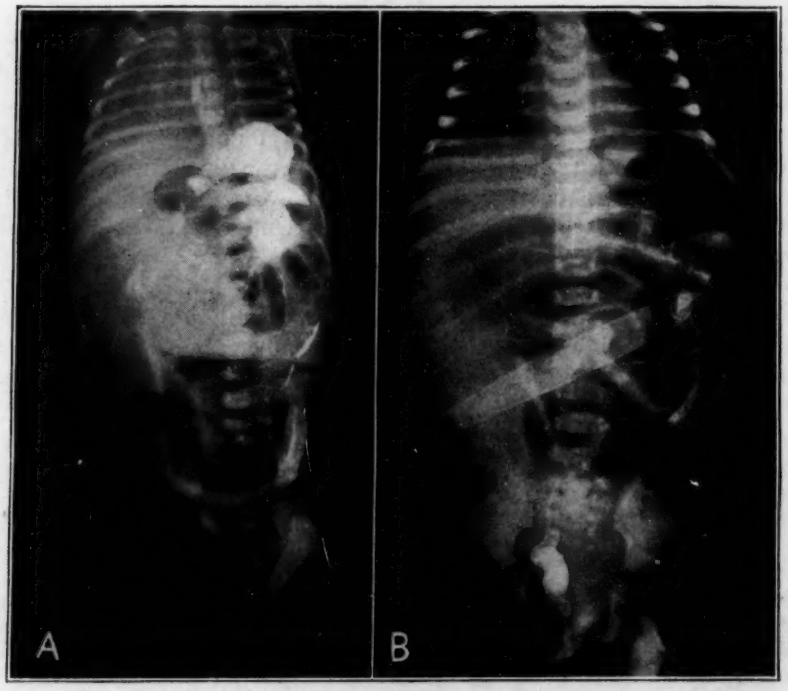

Fig. 1.—Roentgenograms made after introduction of barium sulfate by means of a stomach tube and an enema.

tapered off gradually until it averaged 1 cm. in diameter at the ileocecal valve. The same sticky, green meconium was found also in this portion of the tract. The ileocecal valve was probed and found to be patent. The ascending, transverse and descending portions of the colon were of even smaller diameter than the terminal part of the ileum and contained dry, thick, grayish white meconium which was so firm that it had to be dug out after the intestine was opened. The rectum was somewhat larger and of more normal diameter. Little inspissated meconium was found within its lumen (fig. 2).

The pancreas occupied its usual position and showed no gross abnormalities. Its size, color and consistency appeared to be normal. Since the underlying pathologic change as found later by histologic examination was not recognized at the time of necropsy, the main pancreatic duct was not investigated.

All other viscera were examined but were of no importance as far as the condition of meconium ileus is concerned.

Histologically the most important changes were found in the pancreas. At first glance a striking lobulation of the pancreatic parenchyma was noticed, the lobules being surrounded by a thick layer of loose and edematous fibrous tissue. Often this lobulation resembled the lobula-

tion seen in severe portal cirrhosis of the liver. At this point it was difficult to decide whether the abnormal lobulation was the result of progressive fibrosis, possibly due in part to inflammation, or was the result of faulty development.

Considering the perilobular fibrous tissue first, it was noteworthy that, while the thick bands of connective tissue layers were loose and edematous, only scattered and rare lymphocytes were encountered within it and vascularization did not appear to be abnormally pronounced. In fact, it seemed to be within normal range. Nowhere was there any accumulation of acute inflammatory cells. The perilobular bundles of connective tissue were generally composed of a fine fibrillar network containing an average number of fibroblasts. This histologic appearance was not thought to be that of inflammatory fibrosis. It was remarkable that only in one group

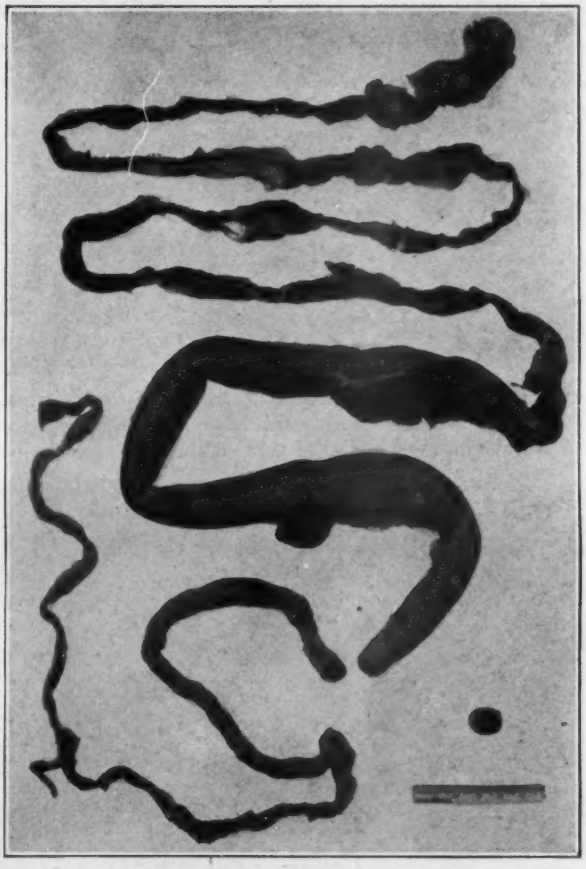

Fig. 2.—Portions of the gastrointestinal tract removed at autopsy.

of sections and in one location was a large excretory duct found. No other fully developed ducts or ductules could be detected in the perilobular connective tissue.

In a study of the lobules themselves a rather unusual picture presented itself. While the acini were abundant, their structure was not normal. In only a few was there orderly arrangement of the component epithelial cells. Often the cells seemed to form curly rows without a lumen, as if budding from a tubular structure. In other areas irregular epithelial cells were grouped together in a circular fashion, sometimes around a space which might well have been a lumen. While it was not possible to find any true ductules with tall columnar epithelium in the parenchyma, small glandlike structures with flattened epithelium were not infrequently found. In some of these a small amount of amorphous eosinophilic material was seen. This could have been exocrine pancreatic secretion. Then again, irregular groups of epithelial cells were found growing like buds into a loose and delicate meshwork of connective tissue fibrils. These delicate fibrils were often seen spreading among the groups of epithelial cells, frequently separating them from each other in a distinct manner. From the histologic

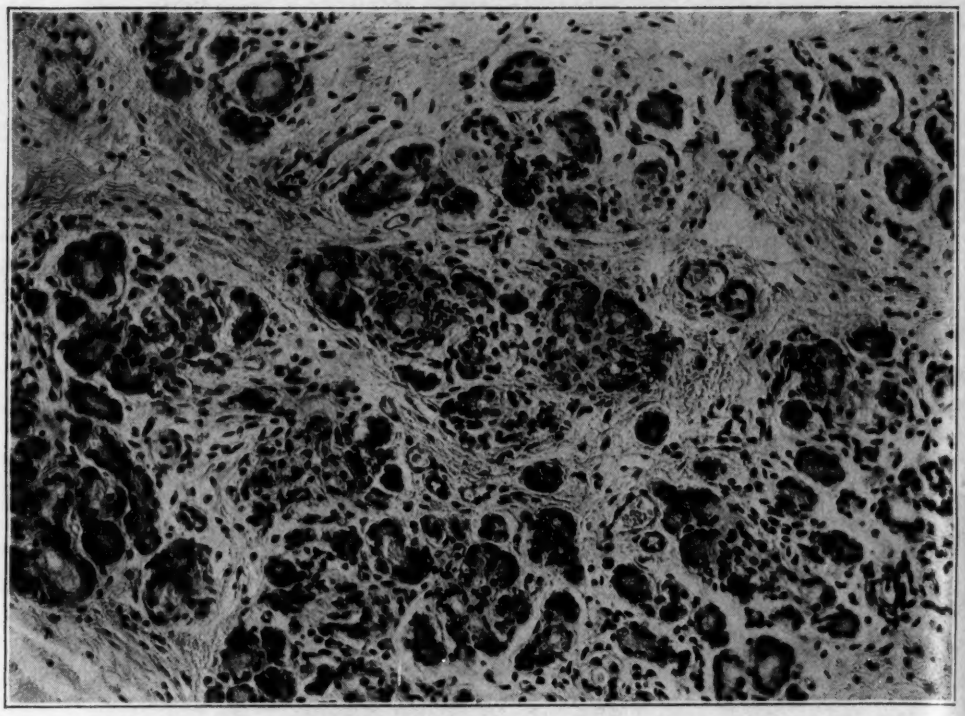

Fig. 3.—Low power photomicrograph, showing the disorderly arrangement of the epithelial elements in the lobules of the pancreas. Note the loose fibrous tissue separating tubular and acinar structures and the clumping of epithelial cells in the center of the photomicrograph.

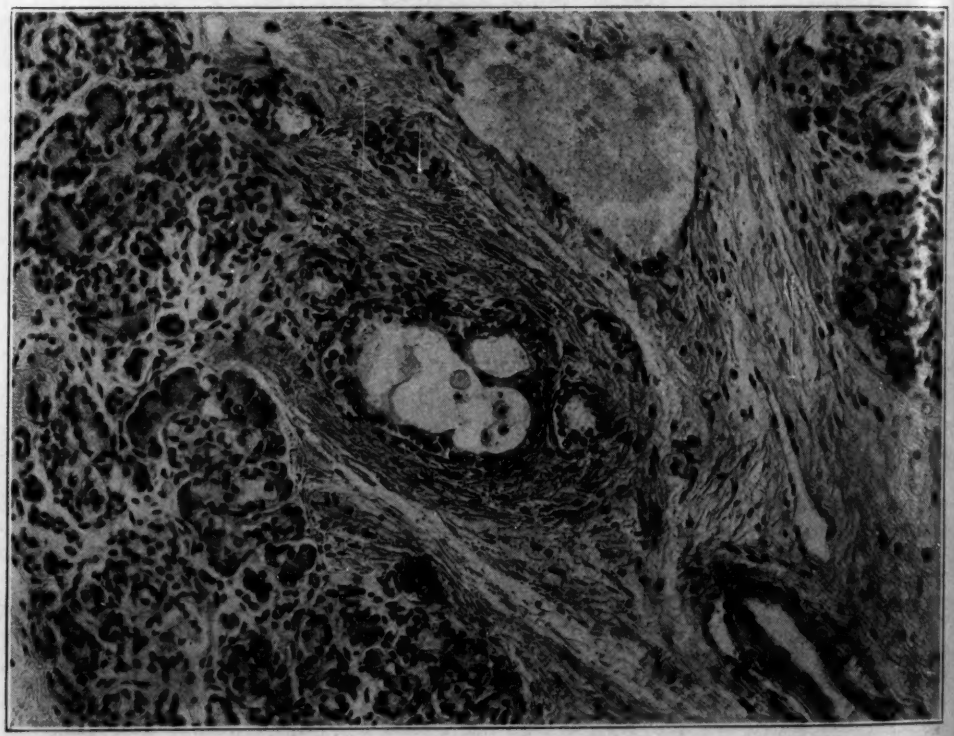

Fig. 4.—Low power photomicrograph, showing a section through the only fully developed duct found in the pancreas.

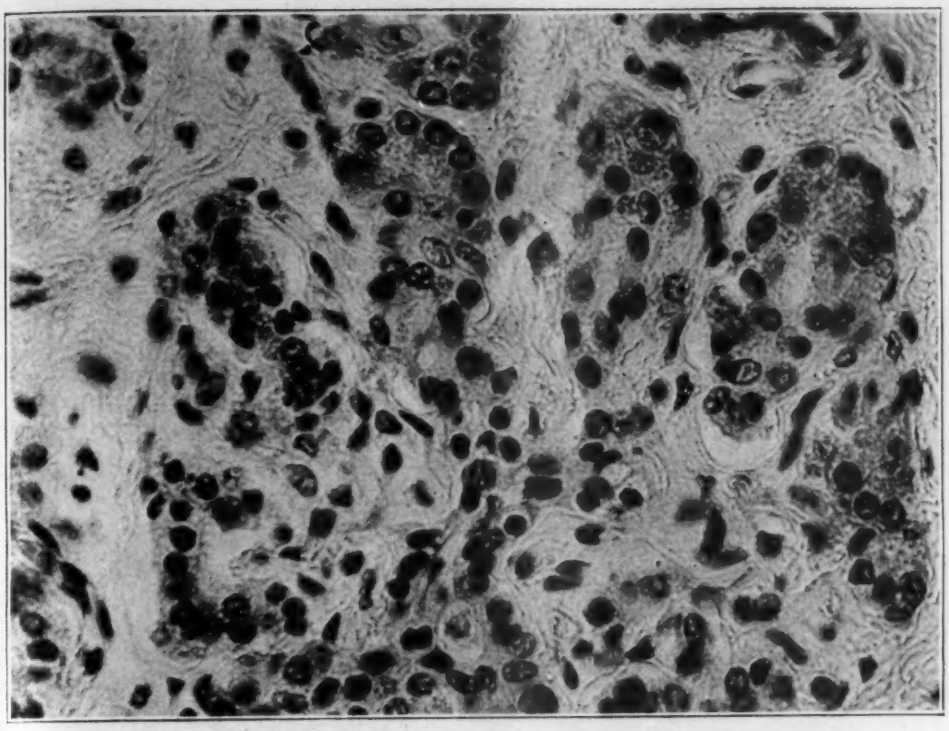

Fig. 5.—High power photomicrograph of a part of a lobule from figure 3. Note the abortive attempt of the epithelial cells to form acini.

Fig. 6.—High power photomicrograph of a part of a lobule from figure 3. This picture illustrates the failure of normal formation of acini. Note the small ductlike structure in the right half of the photomicrograph.

appearance of these sections the impression was gained that the development of the pancreatic acini had been faulty. It appeared that the maturation of ductules into acini had been prematurely arrested and that few mature and normal acini had been laid down. There was no evidence of any inflammatory cells within the parenchyma, and this made an inflammatory origin of this abnormal picture quite improbable (figs. 3, 4, 5 and 6).

Islets of Langerhans were abundant, and although they differed considerably in shape and size no abnormalities could be detected within their component cells.

Except for flattening of the mucosa, the stomach, colon and rectum were not unusual. A section from the ileum which contained the inspissated meconium showed pronounced compression and atrophy of the mucosa, obviously produced by the thick and inspissated meconium. The submucosa formed only a thin strip of compressed tissue lying between the mucosa and the muscular coats. The numerous blood vessels which are normally encountered in the submucosa were greatly compressed and often appeared only as slits filled with a few erythrocytes.

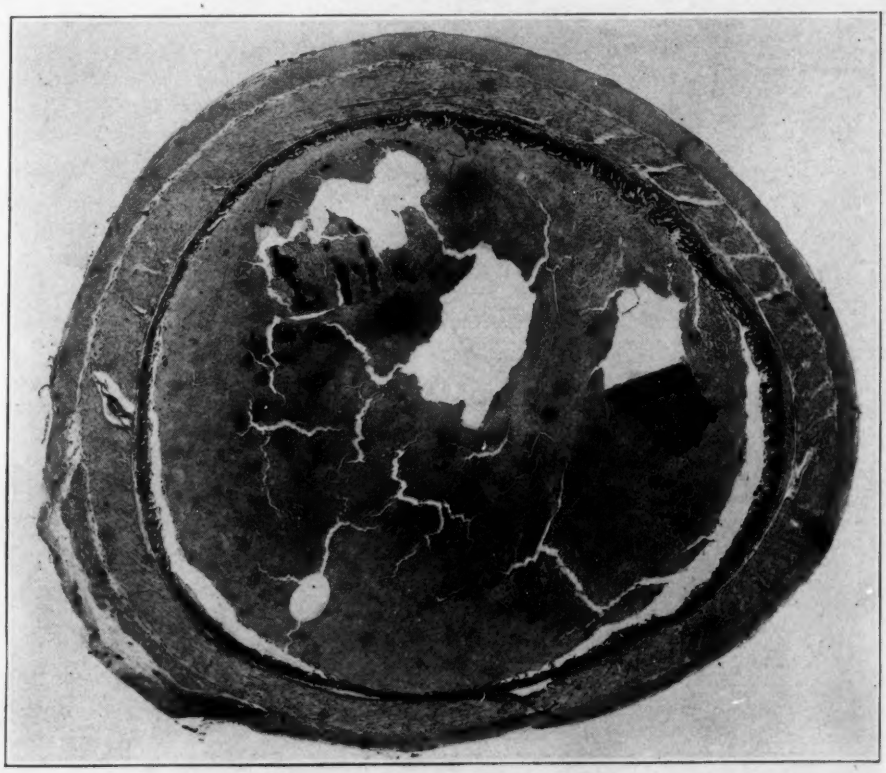

Fig. 7.—Section from the ileum, containing inspissated meconium.

The muscular coats showed in places a slight perivascular edema but were not otherwise unusual (fig. 7).

No abnormal conditions were noted histologically in any of the other organs.

COMMENT, WITH REVIEW OF THE LITERATURE

The observations recorded here are those encountered usually in meconium ileus. This condition was incompatible with life and led to a fatal outcome in this infant within approximately three days. In itself, meconium ileus is not a disease entity but a syndrome brought about by a structural defect in at least one of two vitally important organs. This organ was the pancreas in the case reported here.

It is the object of this study to review critically other cases of this kind and the theories propounded by their authors. It is hoped that this may clarify the important role of the pancreas in the production of meconium ileus.

It was Landsteiner [1] who in 1905 first drew attention to this condition by reporting a case of meconium ileus in a child 5 days of age. This infant died after an illness in which vomiting, abdominal distention and the lack of passage of meconium were the outstanding symptoms. Ileostomy did not relieve the condition. At autopsy, the colon was found to be contracted and the small intestine greatly dilated, up to 7 cm. in diameter in its proximal portion. The lower part of the ileum was filled with a grayish yellow tenacious putty-like mass. There was also a severe peritonitis. Microscopically the pancreas showed extensive fibrosis which did not affect the islets of Langerhans. Unlike our case the pancreatic ducts were present. They were dilated and contained a homogeneous or coarsely granular material which was believed to be inspissated secretion. The largest ductules were in the head of the pancreas. The main pancreatic duct was not enlarged, but near the opening into the duodenum it was "gulflike," with folds in the mucosa. As it approached the pancreas, it became slitlike. The epithelium was desquamated and stained poorly. There was no inflammatory reaction.

Realizing the effect of the pancreatic enzymes on the intestinal contents and their importance in the maintenance of the normal consistency of meconium, Landsteiner concluded that the primary cause of the patient's condition was in the pancreas. He thought that the products of the pancreatic secretions acted on the masses which form the meconium either directly through the intake of fluid or indirectly through secretion, resorption or motor function of the intestinal mucosa.

This theory did not explain satisfactorily the process involved, and it remained for others to analyze the condition further. Landsteiner made one interesting comment, namely, that inspissated meconium was frequently found in infants with congenital syphilis. However, neither in his case nor in ours was there evidence of syphilis in either the mother or the child.

The importance of the lack of the pancreatic enzymes as the main factor responsible for the production of meconium ileus was subsequently stressed by several investigators (Kornblith and Otani,[2] Dodd,[3] Bronaugh and Lattimer,[4] Blackfan and May [5] and Anderson.[6] Kornblith and Otani [2] reported the case of a child who became acutely ill on its third day of life. No meconium was passed. Vomiting and abdominal distention were noted. An operation was performed on the fourth day, and gas was found in the peritoneal cavity. There were a meconium peritonitis and a number of ulcers, which they called distention ulcers. Drainage to the region of the cecum was instituted, but the infant died seventeen hours after the operation and three days after the onset of symptoms.

At autopsy there was a generalized meconium peritonitis. The duodenum and jejunum were dilated, and the intestinal canal was filled with putty-like meconium which was tenacious and adhered firmly to the mucosa. There were five ulcers on the antimesenteric border of the terminal portion of the ileum and a true Meckel diverticulum. There was a perforation in the ascending colon and another just beyond. The colon was distended down to the hepatic flexure. Beyond this it was

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2. Kornblith, B. A., and Otani, S.: Meconium Ileus with Congenital Stenosis of the Main Pancreatic Duct, Am. J. Path. **5**:249, 1929.

3. Dodd, K.: Intestinal Obstruction Due to Meconium Ileus in a Newborn Infant, J. Pediat. **9**:486, 1936.

4. Bronaugh, W., and Lattimer, R. D.: Intestinal Obstruction from Inspissated Meconium, Am. J. Dis. Child. **60**:1371 (Dec.) 1940.

5. Blackfan, K. D., and May, C. O.: Inspissation of Secretion, Dilatation of Ducts and Acini, Atrophy and Fibrosis of the Pancreas in Infants, J. Pediat. **13**:627, 1938.

6. Anderson, D. H.: Cystic Fibrosis of the Pancreas and Its Relation to Celiac Disease: A Clinical and Pathological Study, Am. J. Dis. Child. **56**:344 (Aug.) 1938.

collapsed. The wall was edematous throughout, and diffuse submucosal hemorrhages were seen for 2 cm. in the rectosigmoid.

Microscopically the mucosa of the terminal portion of the ileum was flattened. The tension ulcers were devoid of mucosa, and the musculature was narrowed, hyalinized and necrotic. Meconium was present on the serosal surfaces, but there was no acute inflammatory reaction. The pancreas showed a great increase in stroma. The acinar tissue was generally atrophic and often completely replaced by connective tissue. The pancreatic ducts were dilated and showed extensive proliferation, particularly in the head of the pancreas. The islets of Langerhans were unaffected. The main pancreatic duct was extremely widened and contained a pink-staining substance. The dilatation of the ducts extended even into the terminal portions, involving the acini, with the result that the acinar cells were flattened, occasionally resembling the small duct. There was a small amount of lymphocytic infiltration about the duct in the body of the pancreas. Serial sections through the head of the pancreas showed that the duct of Wirsung was enormously dilated throughout the body and tail, but it decreased in size 600 microns from the duodenal opening, where its wall was thrown into folds and proliferated ducts were found around it. At the region of narrowing, the epithelium was absent and the duct was recognized with difficulty as a narrow slit. It widened slightly from this point to the duodenal opening. The meconium showed many round, hazy fat droplets which stained with sudan III, desquamated epithelial cells and a few cholesterol crystals.

In the opinion of Kornblith and Otani the thick putty-like meconium was responsible for the intestinal obstruction, ulceration and diverticulum formation, the perforation being due to the tension developed in the attempt of the intestine to overcome the obstruction. The changes in the pancreas were almost exactly like those produced by experimental ligation of the pancreatic duct (Ukai[7]).

A new suggestion concerning the cause of the condition was made by Kornblith and Otani, namely that atresia of the pancreatic duct might be the cause of the pancreatic obstruction. Since the major number of intestinal atresias occur in the duodenum and since Tandler[8] explained that the duodenum is especially predisposed to atresias because of the adhesions (Epithelverklebung) during the rotation of the gut in the embryo, Kornblith and Otani expressed the opinion that it was possible for atresia of the pancreatic duct to develop similarly. Thus the outflow of the pancreatic juice into the duodenum would be made impossible, and stasis and damming back of pancreatic secretions would result. Dilatation of ducts and ductules, fibrosis of the parenchyma and atrophy of acini would then be the inevitable outcome.

The importance of the pancreatic exocrine secretions should be considered in the light of certain experiments by Hess.[9] By means of the duodenal bucket method he showed that all three ferments, trypsin, steapsin and amylopsin, are present in infants before they are put to the breast. While the stool of a normal child contains 84 per cent water, the water content of meconium, according to Davy,[10] is only 72 per cent. It ordinarily contains mucus, bile, epithelial cells, fat

7. Ukai, S.: Morphologich-biologische Penkreasstudien, Mitt. ü. allg. Path. u. path. Anat. **3**:1, 1926.

8. Tandler, J.: Zur Entwicklungsgeschichte des menschlichen Duodenums in frühen Embryonalstadien, Morphol. Jahrb. **29**:187, 1900-1902.

9. Hess, A. F., cited by Abt, I. A.: Pediatrics, Philadelphia, W. B. Saunders Company, 1926, vol. 3, p. 26.

10. Davy, J.: On the Composition of Meconium and of the Vernix Caseosa or Lubricating Matter of the Newborn Infant, Med.-Chir. Tr. **27**:189, 1844.

globules, cholesterol and intestinal secretions. Thus meconium is more concentrated in solids than the stool of a child. In Pflüger's [11] opinion, later confirmed by Okada [12] and also by Lombroso,[13] the pancreatic secretion aids in the digestion of fat and in the absorption of fat and proteins from the intestine. Therefore, it was only logical for Kornblith and Otani to conclude that the absence of pancreatic secretions, normally found in the meconium, resulted in the alteration of its consistency because of a deficiency both in dilution of the solids and in the digestion of fats and proteins present.

Dodd's [3] case deserves mention because of its slightly different character and because of the author's conclusions. This infant vomited and passed grayish green to yellow stools resembling thick gelatin. It improved with parenteral fluids and duodenal suction but died of bronchopneumonia on the tenth day of hospitalization (thirteenth day of life). At autopsy the stomach and intestines were distended and the colon was contracted. The lumen of the ileum and the colon were filled with tenacious gray mucoid material similar to the stool. Bile was easily expressed. There was a slight inflammatory reaction of the small intestine with an increased number of mononuclear cells in the mucosa and even below the muscularis mucosa, in the submucosa. The pancreas showed an interstitial pancreatitis with extensive interlobular and intralobular fibrosis. There were some inflammatory cells in the wall of the ducts and in the surrounding fibrous tissue. The ducts and some of the acini were dilated, and many contained a loose, pink, finely granular precipitate. The islets of Langerhans and the remaining acini were normal. No occlusion of the ducts was noted, but stenosis of the main duct was presumed to be present.

Although Dodd expressed the opinion that in meconium ileus some abnormality of the pancreas or even of the liver is always present and therefore probably is the cause of this condition, she pointed out that similar alterations may be found without meconium ileus.

A case reported by Bronaugh and Lattimer [4] in 1940, resembling closely those discussed so far, shows the fallacy of surgical intervention in the presence of meconium ileus. In this infant 61 cm. of ileum containing thick, tenacious, putty-like meconium was removed after symptoms of intestinal obstruction. Partial ileectomy and an end to end anastomosis were done, but the child died on the fourth postoperative day. At autopsy the weight of the pancreas was only 1.5 Gm. (normal 4 to 3.4 Gm.). A large amount of loose fibrous connective tissue was found between the lobules. The acini and smaller ducts were filled with eosin-staining epithelial cells and formless material. Many ducts were dilated. There was some chronic inflammatory reaction in the surrounding connective tissue. In the liver the hepatic cells were pale and granular. Some biliary pigment was present, and some biliferous canaliculi contained small plugs of dark yellowish material.

Blackfan and May,[5] in discussing fibrosis of the pancreas in infants, mentioned 3 infants with intestinal stenosis and meconium ileus, including one set of twins, in 5 infants who died within three weeks after birth. The changes in the pancreas were identical with those reported by Landsteiner, Kornblith and Otani and Dodd,

11. Pflüger, E.: Der gegenwärtige Zustand der Lehre von der Verdauung und Resorption der Fette und eine Verurtheilung der hiermitverknüpften physiologischen Vivisectionen am Menschen, Arch. f. d. ges. Physiol. **82**:303, 1900.

12. Okada, S., and others: Pancreatic Function, Pancreatic Activity in Diabetes Mellitus, Arch. Int. Med. **13**:560 (Aug.) 1928.

13. Lombroso, V.: Zur Frage über die innere Funktion des Pankreas mit besonderer Rücksicht auf den Fettstoffwechsel, Arch. f. exper. Path. u. Pharmakol. **56**:337, 1907.

with extensive fibrosis of the pancreas and pronounced dilatation of the smaller ducts. No gross obstruction of the ducts could be found. The infants who survived the first few weeks showed vomiting, diarrhea, failure to gain weight and chronic infection of the respiratory tract. Some patients also showed evidence of vitamin A deficiency at autopsy. They cited the conclusion drawn by Blackfan and Wolbach (1933) from preliminary studies which indicated that the pathogenesis of this "striking pancreatic affection resides in the production of an abnormal secretion which inspissates and leads to distention and atrophy of the ducts and acini."

Anderson,[6] discussing cystic fibrosis of the pancreas, reported the cases of 5 infants who died before the age of 1 week with intestinal obstruction, 2 with meconium ileus (Landsteiner, and Kornblith and Otani), 1 with a band of fibrous tissue across the lumen of the terminal portion of the ileum and 2 with atresia of the jejunum and ileum. She expressed the opinion that the changes in the pancreas in these cases may be interpreted as a result of obstruction of the small or of the large pancreatic ducts. The stenosis present in some cases may be the result rather than the cause of the pancreatic fibrosis. The smaller ducts were the primary site of obstruction in the majority of cases. Other congenital abnormalities which were observed were atresia and stenosis of epithelium-lined passages, such as the intestine, the cystic duct and the ureters. At times several siblings in the same family were affected.

Congenital malformation, inflammation of the pancreas during fetal life and vitamin A deficiency were stated by Anderson to be the main pathogenic factors. There is experimental evidence that lack of vitamin A may affect the pancreas to a slight degree, and lack of vitamin A in the mother is known to produce a high mortality in fetal and neonatal life. It is known too that a diet low in vitamin A reduces the vitamin A reserves in the young. In the children who died after the first few weeks of life there was evidence of lack of vitamin A.

In the light of the foregoing facts there seems little doubt that the pancreatic lesion in our case, as well as in those discussed, must be considered the cause for the inspissation of the meconium and thus indirectly for the fatal outcome. The lesion itself in our case differs from that in the others in several ways. It is difficult to postulate any occlusion of the main pancreatic duct as being the cause of the pancreatic fibrosis. No inflammation, either active or extinguished, could be found. There was one medium-sized excretory duct, which, however, was not cystic or even dilated. Ductules, or what appeared to be ductules, which were maldeveloped were present among the acini, but they contained little or no secretory material. No dilatation or cyst formation as observed in all other cases so far discussed was found. Thus it appears more probable that a maldevelopment, possibly congenital malformation, of the entire exocrine system is the basic lesion in the present case.

Vitamin A deficiency as the cause of the pancreatic lesion, as proposed by Blackfan and Wolbach [14] and by Anderson, is not apparent in our case. Blackfan and Wolbach's criterion of vitamin A deficiency, namely, squamous metaplasia of the lining epithelium of various parts of the body (trachea, bronchi, renal pelvis and pancreas), was not seen. No examination for vitamin A in the mother was made while she was in the hospital.

Thus it would appear that the cause of meconium ileus was readily established by the finding of obstruction or absence of pancreatic ducts or maldevelopment of

14. Blackfan, K. D., and Wolbach, S. B.: Vitamin A Deficiency in Infants: A Clinical and Pathological Study, J. Pediat. **3**:679, 1933.

the exocrine system. This anatomic disturbance would then lead to lack of the organ's exocrine secretions in the duodenum, where they would exert their beneficial effect on the meconium. While this seems to be the logical conclusion from what we have seen so far, there are several reports in the literature which postulate quite different causes for the development of meconium ileus. It is probably futile to include in a review of the subject such cases, which limit themselves to mere observation of facts without any attempt at interpretation, but they at least deserve acknowledgement. Such are the cases reported by Bullowa and Brennan,[15] Hughes,[16] Adamson and Hild[17] and Meltzer.[18]

A view brought forward by Fanconi,[19] however, is more important, and the case reported by him is extremely interesting.

In 1920 he observed a case of meconium ileus in 1 of twin girls. The infant passed no meconium, refused feedings and vomited meconium-like masses. She died on the third day. At autopsy the intestines were similar to those reported in the preceding cases. The lower portion of the ileum and the colon were of the size of a penholder and were extremely firm. The remainder of the small intestine became gradually dilated and then thinner. The contents of the intestine were putty-like. Only a few drops of clear, slimy fluid appeared at the ampulla of Vater when the gallbladder was compressed. The gallbladder itself contained similar watery, clear, slimy fluid. The biliary ducts could not be probed. The pancreas was normal, both on gross and on microscopic examination. The mucosa of the gastrointestinal tract was compressed, and the meconium feces in the upper jejunum were dark green, which led the author to believe that there was some bile present in the intestine. The liver showed the typical picture of biliary cirrhosis. There was incomplete development of the larger hepatic biliary ducts, which showed more than six epithelial cells around the narrow lumen. There was pronounced and widely distributed fatty infiltration. Serial sections of the biliary ducts showed no displacement of the lumen and no inflammatory changes or cellular infiltration.

In Fanconi's opinion it was the congenital absence of the biliary ducts of the second order which prevented the bile formed in the liver from reaching the intestine, at least in sufficient quantity to be of value. The observed stasis of bile in the liver appeared to corroborate the author's opinion. Realizing that the bile salts are important in the digestion of fats in the intestine, he felt that this digestion was not possible if bile could not reach the duodenum. As to Landsteiner's observation of fibrosis of the pancreas, which was not observed in his own case, he stated the belief that the lack of pancreatic secretion, so important in the splitting and saponification of fats and fatty acids, does not exclude his interpretation. In his opinion lack of either bile or pancreatic enzymes in the intestine of the infant may lead to inspissation of meconium.

While we could not find any other report of a lesion similar to the one described by Fanconi and while in our own case the liver did not show any damage, his theory cannot be absolutely refuted. If malformation of the pancreatic ducts is

15. Bullowa, J. G. M., and Brennan, R. E.: Intra-Uterine Intestinal Obstruction from Inspissated and Impacted Meconium, J. A. M. A. **73**:1882 (Dec. 20) 1919.

16. Hughes, E. E.: Acute Intestinal Obstruction Due to Inspissated Meconium, Brit. J. Child. Dis. **19**:32, 1922.

17. Adamson, E. W., and Hild, J. R.: Meconium Ileus, J. A. M. A. **112**:2275 (June 3) 1939.

18. Meltzer, S.: Meconium Ileus, Canad. M. A. J. **34**:186, 1936.

19. Fanconi, G.: Fünf Fälle von angeborenem Darmverschluss: Dünndarmatresien, Duodenalstenose, Meconiumileus, Virchows Arch. f. path. Anat. **229**:207, 1920.

possible, there is no reason why malformation of hepatic ducts cannot also occur. Certainly the importance of bile in combination with pancreatic enzymes in the digestion of fats and proteins is well known.

Burger's [20] case of meconium ileus in a 72 hour old infant is of interest because no definite changes were found in either the pancreas or the liver. He stated the belief that the underlying cause was an abnormal resorption of water or a decreased quantity or an anomaly of secretion of one of the glands of the digestive tract, particularly the liver or the pancreas. While this theory appears attractive, it lacks any anatomic basis in his own case and has not been confirmed by others.

This review would not be complete without at least a mention of so-called intrinsic factors in the intestine itself, which are supposed to have led to the production of the lesion in a few cases which have been reported. It is questionable, however, whether changes in the pancreas or liver were absent in these cases, since only incomplete autopsies or microscopic examinations were carried out.

Hypoplasia of the lower portion of the ileum and of the colon (Gidionsen, cited by Fanconi [19]), congenital syphilis in the newborn with round cell infiltration of the intestinal wall (Mraček [21]) and even primary dilatation of the small intestine with consequent kinks in the dilated portions of the intestine (Torkel, cited by Burger [20]) were believed to be sufficient cause for the inspissation of meconium. The lack of careful gross and microscopic investigation in these cases casts considerable doubt on the value of conclusions based on them.

It is unfortunate that at the time of necropsy we did not appreciate the nature of the lesion and failed to examine the pancreatic duct at its point of entry into the duodenum. However, careful reexamination of the entire duodenum later failed to show a defect of the papilla of Vater even though the opening of the pancreatic duct could not be found. The biliary ducts were patent. Complete examination of the pancreas in multiple block sections from head to tail established the absence of any intrapancreatic ducts, which makes it at least probable that the larger excretory duct was also absent. Thus the cause of meconium ileus in our own case appears to be similar to that in the cases reported by Kornblith and Otani and others. Nevertheless, the fundamental lesion is somewhat different from that in the cases hitherto reported, in that there was complete maldevelopment of all intrapancreatic ducts, ductules and acini while in all other cases of this type the ducts were present and often cystically dilated (cystic fibrosis). In the latter group there was congenital malformation of the larger pancreatic duct, usually at or close to the ampulla of Vater. The malformation or even absence of all intrapancreatic ducts leads us to believe that in our case there was a congenital atresia of the pancreatic duct system as a whole, arresting the formation of exocrine secretion at the site of its origin.

CONCLUSIONS

The mechanism involved in the production of meconium ileus is thought to be as follows: Obstruction of the larger pancreatic duct, atresia of the pancreatic duct system or malformation of the entire exocrine system prevents the exocrine secretions of this gland from reaching the intestine. Acinar atrophy and fibrosis may result from the two first anomalies. Normal meconium, which is a dark brownish green, semisolid, viscid substance composed of mucus, bile, intestinal

20. Burger, P.: Cas rare d'iléus du nouveau-né par épaississement du méconium, Gynéc. et obst. **37**:176, 1938.

21. Mraček, F.: Über Enteritis bei Lues hereditaria, Vrtljschr. f. Dermat. u. Syph. **10**: 209, 1883.

secretions, fat globules, cholesterol, vernix caseosa, epithelial cells and hair, requires pancreatic enzymes as well as bile for the maintenance of its normal composition and consistency. In case the pancreatic enzymes are lacking in the intestine, a failure of digestion of fats and proteins in the meconium with resulting inspissation and hardening will occur. The tough, semisolid meconium accumulates in the intestine, since normal intestinal peristalsis cannot dislodge it, and fatal intestinal obstruction is the outcome.

SUMMARY

The literature on meconium ileus, a rapidly fatal condition of the newborn infant, is critically reviewed. A case of the condition occurring in a 3 day old infant with a heretofore not described pancreatic anomaly is presented, and the possible causes leading to meconium ileus are discussed.

Dr. Otto A. Faust, Pediatrician in Chief of the Albany Hospital, gave permission for the use of the clinical record of this patient.

Albany Hospital.

Abstracts from Current Literature

Biochemistry; Bacteriology, and Pathology

THE PHOSPHATASE CONTENT OF THE BLOOD PLASMA IN NORMAL AND IN PATHOLOGIC CONDITIONS. ERLING LUNDSTEEN, EMIL VERMEHREN and MARTIN VERMEHREN, Nord. med. (Hospitalstid.) **12**:3711 (Dec. 27) 1941.

The phosphatase content of the plasma is higher in infancy and childhood than in adult age, probably because of the preponderance of phosphatase in connection with the growth of the bones. During puberty there is also an increase of the phosphatase content of the plasma. In the last three months of pregnancy the phosphatase content is constantly increased, and the same holds true in a less degree during lactation. In the first year of life the plasma phosphatase level is subject to seasonal fluctuations, the values being somewhat higher during the winter. In rickets a pathologic increase of the plasma phosphatase level has been demonstrated up to one and a half months before manifest clinical symptoms have occurred.

WALLGREN, Göteborg, Sweden.

Metabolism; Infant Feeding; Milk and Other Foods

CREATINE-CREATININE METABOLISM AND THE HORMONES. HOWARD H. BEARD, JULIA K. ESPENAN, A. LINK KOVEN and PHILIP PIZZOLATO, Endocrinology **29**:722 (Nov.) 1941.

A series of experiments on rats and human beings involving injection or ingestion of water, physiologic solution of sodium chloride with and without creatinine, sodium bicarbonate and disodium phosphate led the authors to suggest the theory that in the presence of water and phosphate creatinine is changed into phosphocreatine, which then serves to supply energy for processes of muscle contraction.

JACOBSEN, Buffalo.

DIETARY REQUIREMENTS FOR FERTILITY AND LACTATION. BARNETT SURE, J. Nutrition **22**: 499 (Nov.) 1941.

According to Sure, a rice bran extract and a liver extract were found to supply an organic B_x factor which resulted in successful lactation in 90 per cent of cases. Paraaminobenzoic acid and inositol are suggested components of this new factor.

FREDEEN, Kansas City, Mo.

THE INFLUENCE OF PRENATAL DIET ON THE MOTHER AND CHILD. J. H. EBBS, F. F. TISDALL and W. A. SCOTT, J. Nutrition **22**:515 (Nov.) 1941.

Ebbs, Tisdall and Scott found that in addition to other important factors for a successful outcome of pregnancy the nutrition of the mother during the prenatal period considerably influenced the whole course of pregnancy as well as directly affected the health of the child during the first six months of life.

FREDEEN, Kansas City, Mo.

A STUDY OF SONIZED SOFT CURD MILK PREPARED FROM CERTIFIED MILK: REPORT OF A SPECIAL COMMITTEE FROM THE MILK COMMISSION OF THE MEDICAL SOCIETY OF THE COUNTY OF KINGS TO THE NEW YORK DEPARTMENT OF HEALTH. New York State J. Med. **41**:2052 (Oct. 15) 1941.

A new method of lowering the curd tension of milk, called the sonic process, gives much the same results as homogenization. This method was used to homogenize certified milk. "In this method the milk is passed slowly at no pressure over a magnetically driven plate vibrating intensely with the frequency of sound waves. Effective curd tension lowering results." It is now possible to secure milk that has all the advantages of certified milk and which has also been homogenized.

The article does not state whether the milk is pasteurized. A better taste, a lower curd tension, a lower bacteria count and a normal butterfat content are claimed as advantages over regular pasteurized milk. A series of cases are reported in which good results were obtained from its use. The milk was used for small infants. The children seemed more comfortable when fed on sonized certified milk.

AIKMAN, Rochester, N. Y.

INADEQUACY FOR MICE OF A SYNTHETIC DIET SUPPLEMENTED WITH ALL KNOWN VITAMIN B FACTORS. ELIZABETH TROESCHER-ELAM and HERBERT M. EVANS, Proc. Soc. Exper. Biol. & Med. **48**:549 (Dec.) 1941.

Twenty-four 21 day old male mice when fed a ration of extracted casein, sucrose, salts, cod liver oil, corn oil and butter fat and given thiamine, riboflavin, pyridoxine, nicotinic acid, calcium pantothenate, choline, ascorbic acid, inositol and paraaminobenzoic acid, grew well but failed to have good coats of fur. When supplements of fresh beef liver were given, there were increased rate of growth and improvement of the appearance of the fur. Concentrates of liver extract had similar effects but not so good. Pimelic acid had no effect.

HANSEN, Minneapolis.

NITROGEN BALANCE IN EXPERIMENTAL TRYPTOPHANE DEFICIENCY IN MAN. L. EMMETT HOLT JR., ANTHONY A. ALBANESE, JOSEPH E. BRUMBACK JR., CHARLOTTE KAJDI and DOROTHY M. WANGERIN, Proc. Soc. Exper. Biol. & Med. **48**:726 (Dec.) 1941.

Four normal men were maintained on a diet deficient in tryptophan for two to five weeks. Only 10 per cent of the nitrogen was from food; the other 90 per cent was obtained from an acid hydrolysate of casein to which 1 per cent of cystine was added. All subjects went into a negative nitrogen balance when tryptophan was withheld from the diet, and nitrogen equilibrium was restored within a week after tryptophan was again administered.

HANSEN, Minneapolis.

NITROGEN BALANCE IN EXPERIMENTAL LYSINE DEFICIENCY IN MAN. ANTHONY A. ALBANESE, L. EMMETT HOLT JR., JOSEPH E. BRUMBACK JR., MAJORIE HAYES, CHARLOTTE KAJDI and DOROTHY M. WANGERIN, Proc. Soc. Exper. Biol. & Med. **48**:728 (Dec.) 1941.

Five human subjects were maintained on a diet deficient in lysine for two to five weeks. A negative nitrogen balance developed, which disappeared when lysine was again supplied. In a woman the negative nitrogen balance disappeared just before the onset of menstruation. The menstrual flow was scanty, and premenstrual distress and signs of swelling of the breasts, headache and gain in weight usually experienced by this patient were absent when she was on the lysine-deficient diet.

HANSEN, Minneapolis.

CONTRIBUTION TO THE PATHOLOGY AND TREATMENT OF THE WASTING INFANT. STEFAN ENGEL, Brit. J. Child. Dis. **38**:123 (Oct.-Dec.) 1941.

The author stresses the importance of respiratory impairment in wasting infants. Hitherto attention has been focused chiefly on intestinal and metabolic disturbances. His own investigations have revealed that a close relationship exists between the thorax and the lungs. The early growth of the lungs and the differentiation of their tissue are arrested if the thorax stops growing. Measurement of the chest of normal infants has shown that growth is most rapid during the first three or four months. As a result of arrest of pulmonary growth the pulmonary volume of wasting infants proves to be small and the progress of growth slow. Metabolism and circulation are impaired by the defective respiration, and this impairment in turn reacts unfavorably on the respiration. A vicious circle results.

Of major importance in the treatment of these infants must be considered measures that promote better respiration, such as hot baths combined with douches of tepid water, administration of oxygen or carbon dioxide and open air treatment. Blood transfusion may be helpful.

LANGMANN, New York.

NUTRITION OF RURAL CHILDREN IN WAR TIME. DAGMAR CURJEL WILSON, Lancet **2**:405 (Oct. 4) 1941.

The nutritional state of 499 rural Oxfordshire school children was determined in December 1939, before the introduction of rationing, and again in April 1941, after more than a year of dietary restrictions. There was no sign of increasing nutritional deficiency and no deterioration in the state of nutrition as assessed by the same observer. Some degree of vitamin B_2 (riboflavin) deficiency was present in 17 children, as indicated by the presence of angular stomatitis (cheilosis).

LANGMANN, New York.

LACTATION LASTING MANY YEARS WITH ABNORMAL MILK COMPOSITION: REPORT OF A CASE. E. FREUDENBERG, Ann. pædiat. **157**:241, 1941.

A report is given of the composition of the milk of a psychotic woman, who for more than four years emptied her breasts manually. The milk was exceptionally rich in fat, albumin and ash; however, casein and other typical milk components were absent or showed only traces.

AUTHOR'S SUMMARY.

Vitamins; Avitaminoses

THE VALUE OF MEAT AS AN ANTISCORBUTIC. VICTOR E. LEVINE, Am. J. Digest. Dis. **8**:454 (Dec.) 1941.

This historical review is a most interesting common sense article, stressing the antiscorbutic value of fresh meat. Time elapsing between slaughtering and consuming of the meat decreases the content of ascorbic acid. The clinical test of arctic and antarctic expeditions reveals that no scurvy ever occurred when the men lived off the land and killed their own meat.

A factor other than vitamin C, or ascorbic acid, plays a part in the bleeding tendency and probably also in scurvy. This vitamin P, or the permeability factor, occurs in large quantities in orange peel and lemon peel and probably in the covering of many fruits and vegetables.

Many other practical sources of ascorbic acid are stressed, such as germinating seeds, pine needles, sassafras, leaves and twigs of spruce and fir and the common garden variety of freshly cut grass.

MORRISON, Savannah, Ga.

THE GENESIS OF PELLAGRA, PERNICIOUS ANEMIA AND SPRUE. SEALE HARRIS and SEALE HARRIS JR., Am. J. Digest. Dis. **9**:29 (Jan.) 1942.

This most interesting article reviews much of the clinical investigation of pellagra, pernicious anemia and sprue. Although they are distinct and separate entities, they appear to be allied nutritional diseases.

MORRISON, Savannah, Ga.

THE OXYGEN CONSUMPTION, CREATINE, AND CHLORIDE CONTENT OF MUSCLES FROM VITAMIN E–DEFICIENT ANIMALS AS INFLUENCED BY FEEDING α-TOCOPHEROL. O. B. HOUCHIN and H. A. MATTILL, J. Biol. Chem. **146**:301, 1942.

Dystrophic muscle from vitamin E–deficient animals as compared with muscle from normal animals has a much higher oxygen consumption, a somewhat lower creatine content and a higher chloride content. Dystrophic hamster muscle showed the most striking increased oxygen consumption, 250 per cent of the normal. The oxygen consumption rate of paralyzed nursing rats was 160 per cent of normal. Oxygen uptake appeared to increase with the severity of the dystrophic condition. The creatine content was variably decreased, but not greatly except in slowly developing, severe dystrophy. Oral administration of alpha tocopherol to the dystrophic hamster resulted in the lowering of oxygen consumption toward the normal within twenty-seven hours. The chloride content remained high even after forty-eight hours. Biopsies on the rabbit demonstrated conclusively that alpha tocopherol acetate given by mouth lowered the high initial oxygen consumption of the muscle toward normal, and in as short a time as ten hours. The concentration of creatine was not significantly altered, and the chloride content remained high. Neither the operation nor the anesthesia had any effect on the oxygen consumption or the creatine content of muscle of normal animals.

PAGE, Indianapolis [ARCH. NEUROL. & PSYCHIAT.].

DARK ADAPTOMETER AND BLOOD VITAMIN A MEASUREMENTS IN A NORTH CAROLINA NUTRITION SURVEY. M. E. YARBROUGH and W. J. DANN, J. Nutrition **22**:597 (Dec.) 1941.

Yarbrough and Dann concluded that the blood level of vitamin A is the most satisfactory single test for the detecting of a mild avitaminosis A. However, more data are needed to establish a range of normal and abnormal values.

FREDEEN, Kansas City, Mo.

STUDIES IN NICOTINIC ACID: I. THE FATE OF NICOTINIC ACID IN MAN. HERBERT P. SARETT, JESSE W. HUFF and WILLIAM A. PERLZWEIG, J. Nutrition **23**:23 (Jan.) 1942.

The two known end products of nicotinic acid metabolism found in human urine are trigonelline and nicotinuric acid. A diet free of coffee, peas, beans and other legumes was used by Sarett and associates for the study of normal excretion of trigonelline in man. The 3 subjects tested with such a rigorously controlled diet excreted 9 to 13 mg. of trigonelline per day. On a less controlled diet, 26 students excreted an average of 15 mg. per day. Three subjects after fasting for three days excreted 8 to 12.6 mg. per day.

Thirty-six subjects with different diets and under fasting conditions excreted daily 0.7 to 2.2 mg. of acid-hydrolyzable nicotinic acid derivatives. Smoking did not affect this level.

Regardless of the diet there was a constant loss of at least 10 mg. of known nicotinic acid derivatives in the urine.

Trigonelline was not utilized by human subjects when taken orally and was excreted almost completely unchanged. Nicotinuric acid when ingested was excreted to the extent of about 50 per cent unchanged, without an accompanying increase in trigonelline.

It was suggested that after a test dose of nicotinic acid amide, the extra excretion of acid-hydrolyzable nicotinic acid derivatives and trigonelline may be used as an indication of the nutritional status of a patient with respect to nicotinic acid.

FREDEEN, Kansas City, Mo.

THE PANTOTHENIC ACID CONTENT OF ROYAL JELLY. P. B. PEARSON and C. J. BURGIN. Proc. Soc. Exper. Biol. & Med. **48**:415 (Nov.) 1941.

Both worker and queen bees derived from female larvae of the honey-bees are reared on royal jelly, a secretion of the pharyngeal glands of the workers, for the first two days. On the third day the diet of the workers is changed, while the members of the queen caste continue to receive royal jelly. Assays of fresh royal jelly by microbiologic method (Jukes, T. H., *J. Nutrition* **21**:193, 1941) disclosed an unusually large content of pantothenic acid (average 511 micrograms per gram of dry weight). This substance (royal jelly) is 2.5 to 6 times as rich in this vitamin as yeast or liver. It is not yet known whether the high pantothenic acid content in royal jelly is the significant dietary factor which causes certain larvae to develop into queens.

HANSEN, Minneapolis.

URINARY EXCRETION OF PANTOTHENIC ACID BY NORMAL INDIVIDUALS. LEMUEL D. WRIGHT and ERNESTINE Q. WRIGHT, Proc. Soc. Exper. Biol. & Med. **49**:80 (Jan.) 1942.

The mean daily excretion of pantothenic acid determined by the method of Pennington, Snell and Williams (*J. Biol. Chem.* **135**:213, 1940) on 57 samples of urine from 24 normal persons was 3.42 mg., with a maximum of 5.54 and a minimum of 1.10 mg.

HANSEN, Minneapolis.

POSSIBLE ARIBOFLAVINOSIS IN A PREMATURE INFANT. STUART S. STEVENSON, Yale J. Biol. & Med. **14**:403, 1942.

On the thirteenth day of life, a 1,990 Gm. infant showed symmetric honey-colored crusting about the mucocutaneous border of her mouth and a tiny similar lesion at the right nostril. The baby was artificially fed on a cow's milk and dextrimaltose mixture and continued to gain weight and do well during the entire stay in the hospital. The crusting increased in degree for two days, at which time administration of riboflavin, 3 mg. by mouth per day, was begun and continued for three days. After twenty-four hours of therapy, the crusting had largely disappeared.

It is suggested that this may have been a case of ariboflavinosis, and the author points out that human milk and cow's milk are borderline in their satisfaction of the infant's needs for riboflavin.

STEVENSON, New Haven, Conn.

THE THIAMIN (VITAMIN B_1) CONTENT OF HUMAN MILK. E. C. SLATER and E. J. RIAL, M. J. Australia **1**:3 (Jan. 3) 1942.

The thiamine content of normal human milk, as reported by Slater and Rial, increases from a value of 9.5 micrograms per hundred cubic centimeters in the third week of lactation to a maximum of 14,8 micrograms in about the twentieth week, after which time it remains almost constant. In 60 per cent of cases breast milk of mothers whose infants suffer from failure to gain in weight at a normal rate, constipation or vomiting contains substandard amounts of thiamine. The low thiamine content of milk during early lactation suggests that the infant is born with reserves of the vitamin. Although the thiamine content of human milk is dependent on thiamine intake, it is impossible to raise it beyond a certan level (about 20 micrograms per hundred cubic centimeters) by administering large quantities of the vitamin. The authors suggest that the marginal requirement of the breast-fed infant for thiamine is 0.36 microgram for each nonfat calory and that the optimal requirement is not greater than 0.62 microgram for each nonfat calory.

GONCE JR., Madison, Wis.

THE DETERMINATION OF THE THIAMIN (VITAMIN B_1) CONTENT OF THE DIET OF SERVICE PERSONNEL IN TRAINING. M. V. BAINTON and E. C. SLATER, M. J. Australia **1**:135 (Jan. 31) 1942.

Complete daily servings of food prepared for military service personnel in training were analyzed for thiamine by the thiochrome method. The average daily intake per man was

found to be as follows: thiamine, 0.9 mg. (300 U. S. P. units); protein, 106 Gm.; carbohydrate, 286 Gm.; fat, 119 Gm., and calories, 2,704. The ratio of thiamine to nonfat calories was 0.56. The agreement between the values obtained by laboratory methods and those calculated from the food purchases was close. Inasmuch as the carbohydrate and total calorific intake were low and the nutrition of the men excellent, it is believed that the deficiency of calories was made up by the ingestion of food other than that provided by the regular meals. Evidence was obtained to support the belief that these extra foods were carbohydrate, poor in thiamine, and consequently it is thought that the average ratio of thiamine to nonfat calories might be reduced to about 0.47.

GONCE JR., Madison, Wis.

Hygiene; Growth and Nutrition; Public Health

ANTHROPOMETRIC AND ORTHOPEDIC EXAMINATIONS: A TECHNIQUE FOR USE WITH CHILDREN. MABEL POTTINGER BAUM and VERNETTE S. VICKERS, Child Development **12**:339 (Dec.) 1941.

There is an inescapable error in the taking of measurements on living subjects, but this error can and must be kept within reasonable limits if the usefulness of measurements in revealing the progress of growth is not to be lost. Baum and Vickers have studied the problems involved in the evaluation of body size and rate of growth and the study of body proportions and relationships in children throughout the first ten years of life, and in this article they submit practical suggestions as to how inaccuracies may be guarded against, while at the same time fatigue, boredom and fear for the child are avoided. They recognize the important influence of psychologic factors and give detailed suggestions as to how to meet them with children of different ages.

Carelessness in measuring children is commonly countenanced by physicians and others who are precise in the application of laboratory and other technics. This is possibly because of lack of conviction that the former have practical value, but the accumulating evidence of the interpretative value of accurate and repeated measurements is impressive. It requires little more time or effort to take measurements carefully according to a planned and precise technic than in a careless or changeable manner, and data obtained in the latter manner have no value. The authors have rendered all persons interested in the observation of growth a real service in making definite suggestions as to how they may facilitate and improve their procedures for obtaining measurements. Even though the clinician will not obtain all the data referred to in the article, the recommendations made will prove of value in connection with the taking of but a few.

STUART, Boston.

THE DEGREE OF UNDERPRIVILEGE IN DEPENDENT CHILDREN. RAYMOND R. WILLOUGHBY, Child Development **12**:369 (Dec.) 1941.

The federal government sponsors a relief program for children deprived of support by reason of the death, incapacity or continual absence of parents. Such of these ("ADC") children as were in school in the city of Providence, R. I., in February 1941 and a control for each child (the next non-ADC child of the same sex in the alphabetical schoolroom list) were studied with respect to number of siblings, intelligence quotient, school marks and teachers' notations on health and discipline. It was found that the ADC children come from somewhat larger families, are about two points inferior in intelligence quotient, receive lower school marks and are more frequently noted unfavorably by the teachers with respect to health and discipline. These differences are significant and appear to be independent of each other. It is unlikely that they spring from prejudice on the part of teachers, since normally the latter are unaware of the relief status of the children. Since the home broken by death or desertion preponderates in the principal material, work has been started, since the report here abstracted, on the submaterial consisting of children in homes where the father, though incapacitated, is present; in this material the family size difference remains as before, the intelligence difference is reversed and the other differences are reduced to negligible size. The conclusion is suggested that the original differences are a function of the broken home rather than of the relief status.

FROM THE AUTHOR'S SUMMARY.

THE ROLE OF THE MOTHER IN THE HOSPITALIZATION OF THE INFANT. J. BONABA and M. L. SALDUN DE RODRIGUEZ, Arch. de pediat. d. Uruguay **13**:9 (Jan.) 1942.

The role of the hospital should really be a dual role—first to function as an agency for the relief of the sick person and second to function as an agency which gives assistance to the medicosocial aspect of the case and teaches prophylaxis. In hospitals for children the latter function is almost more important than the first.

The modern hospital for children is truly a center of prophylaxis. It is actually an institute of puericulture and a center where all types of child and maternal welfare are practiced. This is particularly the role of the outpatient department of such an institution.

The author feels that hospitalization of the infant should approximate as much as possible the conditions of the home; i. e. the infant should, if possible, be hospitalized with his mother. By this procedure it is possible to retain and implement all the beneficial psychologic factors which operate in the care of an affectionate mother for the child.

Various objections which may arise are not of practical importance and can be diminished considerably through good organization. When the advantages and disadvantages of such a procedure are compared, the scale is all in favor of the advantages. SCHLUTZ, Chicago.

PEDIATRICS IN RELATION TO MEDICINE AND SOCIAL HYGIENE: HISTORICAL OUTLINE. GREGORIO ARAOZ ALFARO, Bol. Inst. internac. am. de protec. a la infancia **15**:365 (Jan.) 1942.

It is not easy to summarize this lecture, for it is a detailed historical outline which embraces the study of social medicine and hygiene from ancient times down to our own day. In a final synthesis the author shows how pediatrics, which at the beginning was only the art of healing, is every day becoming more social and preventive.

[FROM THE EDITOR'S SUMMARY.]

THE VIII INTERNATIONAL CONFERENCE "NEW EDUCATION FELLOWSHIP," ANN ARBOR, MICHIGAN, U. S. A. RAMON I. CARDOZO, Bol. Inst. internac. am. de protec. a la infancia **15**:420 (Jan.) 1942.

The conference widely attained the four objects borne in mind by the Progressive Education Association, which are: to give an opportunity to the teachers of the American Continent to know one another; to strengthen in Latin American educators, especially among the followers of the new education, their faith in the social and pedagogic value of it; to make known American culture; to intensify the good neighborhood policy in order to strengthen the moral bonds among the educators of the mind. The author graphically describes the interest awakened by the lectures given by John Dewey, Washburne, Parkhurst and Kilpatrick as well as by the classes which the visitors attended at different educational establishments, especially at Columbus (Ohio), Columbia University (New York), Teachers College, Lincoln School and Little Red School, in many of which with real success different methods of the new education, such as the method of projects and the Winnetka and Dalton Plans. are applied.

[EDITOR'S SUMMARY.]

Prematurity and Congenital Deformities

WEBBING OF THE AXILLARY REGION. CHARLES J. SUTRO, Bull. Hosp. Joint Dis. **3**:32 (Jan.) 1942.

Two instances of webbing of the axillary region, one bilateral and the other unilateral but both associated with musculoskeletal anomalies, are cited. The abnormal flaps of skin may be overlooked, especially when concomitant muscular atrophy is pronounced, and the patient may be treated for a primary muscular dystrophy. Surgical operation on the web and the contiguous short muscles may improve the range of abduction of the affected extremities in certain subjects. It is noted that the absence of subcutaneous ligaments also plays a part in the production of some cutaneous webs.

FROM THE AUTHOR'S SUMMARY.

OXYCEPHALY. JOSEPH E. J. KING, New York State J. Med. **41**:2119 (Nov. 1) 1941.

Four cases of oxycephaly are reported in which a plastic operation on the skull relieved the deformity to a certain extent and improved the vision and mentality. In this operation the skull is cut in a checkerboard or mosaic plan, by which the deformity is decreased and the pressure relieved. The physical and mental improvement occurs early after the operation. The operation is not recommended for patients with microcephaly or for idiots.

AIKMAN, Rochester, N. Y.

CLINICAL FETAL ELECTROCARDIOGRAPHY: ITS PRACTICAL ACCOMPLISHMENT. ARTHUR J. GEIGER, WILLYS M. MONROE and ALLAN V. N. GOODYER, Proc. Soc. Exper. Biol. & Med. **48**:646 (Dec.) 1941.

By using a single stage resistance-coupled amplifier with a conventional portable electrocardiograph the authors obtained the current of the fetal heart during the last two months of

pregnancy in all instances, usually in the seventh month. This should aid in the differential diagnosis of pregnancy from abdominal tumors and serve as proof of life of the fetus.

HANSEN, Minneapolis.

THE SECRETION OF URINE BY PREMATURE INFANTS. W. F. YOUNG, J. L. HALLUM and R. A. MCCANCE, Arch. Dis. Childhood **16**:243 (Dec.) 1941.

The serum chemistry (urea, sodium chloride and protein) of 19 premature infants was studied.

There were three groups: (1) infants aged 3 to 5 days; (2) edematous infants aged 2 to 7 days, and (3) infants aged 8 to 18 days.

Chemical studies of the urine of these infants enabled the authors to summarize as follows:

"(1) As in full-term infants the urea clearances and probably the glomerular filtration rates vary extensively with the minute volume.

"(2) Making surface area the basis of comparison, premature infants have lower urea clearances than full-term infants, but their sodium and chloride clearances are still more reduced, so that they have smaller $\frac{\text{sodium}}{\text{urea}}$ and $\frac{\text{chloride}}{\text{urea}}$ clearance ratios. It has been suggested that this underlies the tendency of premature infants to get oedema.

"(3) The osmotic pressure of the urine of premature infants is generally very low and the U/P ratio is seldom over 1. The ratio may rise above 1 if the blood urea is high.

"(4) Infants with oedema consistently excrete small volumes of urine, but their urea and mineral clearances are no lower than those of their 'normal' fellows at comparable minute volumes.

"(5) Broadly speaking, the functional differences between adults and full-term infants are exaggerated in premature infants."

KELLY, Milwaukee.

A SIMPLE SAFEGUARD IN THE FEEDING OF PREMATURE INFANTS. K. CAMPBELL, M. J. Australia **1**:76 (Jan. 17) 1942.

In an endeavor to steer a safe course between the dangers of overfeeding and those of underfeeding the premature infant the following routine formula has been evolved by the author and has been found satisfactory: ounces of food per pound of body weight per day on the first day of life, 0.5; on the second day, 1.0; on the third day, 1.5; on the fourth day, 2.0; on the fifth day, 2.5; on the sixth day and thereafter 3.0. The foods used are breast milk and a suitable artificial food containing 20 calories per ounce. Feedings are started at the age of 6 hours and are given every three hours by tube. An attempt at aspiration of the gastric contents is made at each insertion of the tube, and any residue from the previous feeding is withdrawn and measured and the amount of feeding being given at the time reduced by an amount equivalent to the residue obtained. Usually, however, there is no residue.

GONCE JR., Madison, Wis.

PREMATURE INFANTS. GERT VON SYDOW, Svenska läk.-tidning. **38**:2631 (Dec. 5); 2715 (Dec. 12) 1941.

The author gives a description of the mode of care of premature infants at the premature department of the municipal lying-in hospital at Göteborg, Sweden. He stresses the importance of differentiating prematurity, congenital debility and underweight (birth weight less than 2,500 Gm.). About a third of the infants with a birth weight less than 2,500 Gm. had a fetal age of more than 36 weeks. The premature infants constituted 5 per cent of all living newborn children in Göteborg. The author discusses at some length the causes of premature birth and stresses especially toxicosis and bleeding during pregnancy. Premature children should be cared for in special departments for premature infants at the maternity hospitals; they should be given breast milk, a prophylactic dose of vitamin K and daily doses of vitamin D from the first day of life.

WALLGREN, Göteborg, Sweden.

Newborn

EPIDEMIC NEONATAL DIARRHEA IN MATERNITY HOSPITALS; I. CLINICAL ASPECT. GEORGE ORMISTON, Lancet **2**:588 (Nov. 15) 1941.

The purpose of this paper is to summarize the results of studies on the nature of three outbreaks of diarrhea confined to newborn infants during the latter half of 1940 in maternity hospitals serving three widely separated cities in England.

Of a total of 996 infants born during this period in these three hospitals, 139 were affected, and of these 41 died (29 per cent).

All three outbreaks occurred during the summer. The incubation period was probably short, from one to eight days. Most of the infants became ill within the first week of life. No evidence was discovered among the medical or other staff of colds, influenza, furuncles or digestive disturbances that might be regarded as a possible cause.

Routine bacteriologic cultures of material from the throat and of stools of infants, mothers, medical staff and domestic staff were not revealing. Postmortem examinations on 17 of the infants showed no change of note.

It is important that the nature of these outbreaks should be recognized early and the hospital closed at once.

LANGMANN, New York.

EPIDEMIC NEONATAL DIARRHEA IN MATERNITY HOSPITALS: II. BACTERIOLOGICAL ASPECT. NUALA CROWLEY, FORREST FULTON, A. W. DOWNIE and G. S. WILSON, Lancet **2**:590 (Nov. 15) 1941.

Study of 57 normal noncontact breast-fed infants, 3 to 23 days of age, in maternity homes free of neonatal diarrhea showed that cultures of the stools grew organisms in the following proportion: lactic acid bacilli (Lactobacillus bifidus) 80 per cent, coliform bacilli 10 per cent and streptococci and staphylococci each about 4 per cent.

Infants with neonatal diarrhea (studied in two outbreaks) had these organisms in their stools: lactobacilli 30 to 60 per cent and coliform bacilli 55 to 31 per cent respectively. However, similar changes were found in healthy control contact patients during the same outbreaks.

No organisms of the salmonella or dysentery groups were found, and no evidence was obtained of the existence in the stools of soluble toxins for mice. In one outbreak Staphylococcus aureus was isolated from the milk of a number of mothers with sick children (but none of the strains formed an enterotoxin). However in another outbreak four strains that were coagulase-positive, hemolysin-positive and enterotoxin-positive were isolated from cow's milk.

LANGMANN, New York.

VITAMIN K AND PROTHROMBIN CONTENT OF BLOOD IN NEWBORN. M. ROUHUNKOSKI and N. SAKSELA, Nord. med. (Finska läk.-sällsk. handl.) **12**:3007 (Oct. 25) 1941.

Determinations of the prothrombin level of the plasma of 74 full term and 15 premature newborn infants during the first ten days of life were made. The reports of American and Scandinavian authors were confirmed. In premature infants a greater decrease of the prothrombin level of the plasma was found than in full term babies. The hypoprothrombinemia was extreme in children whose mothers suffered from nephrosis during pregnancy. The individual fluctuations of the prothrombin level were considered due to differences in the permeability of the placenta. By administration of vitamin K to the mother some hours before delivery or to the infant immediately after birth the hypoprothrombinemia almost always could be prevented.

WALLGREN, Göteborg, Sweden.

Acute Contagious Diseases

MYOCARDIAL NECROSIS IN DIPHTHERIA. K. Y. CH'IN and C. H. HUANG, Am. Heart J. **22**:690 (Nov.) 1941.

Extensive myocardial necrosis was found in the heart of a child who succumbed to diphtheria on the seventeenth day of the disease. The authors call attention to the relative rarity of extensive necrosis of the heart muscle in fatal diphtheria. The literature relative to circulatory failure in diphtheria is reviewed, and the various views which have been brought forward to explain the cause of the cardiac failure are discussed.

GIBSON, Chicago.

THE INTRODUCTION OF THE PRACTICE OF VACCINATION INTO NAPOLEONIC FRANCE. ROBERT G. DUNBAR, Bull. Hist. Med. **10**:635 (Dec.) 1941.

Because of the war between England and France the scientific intercourse between the two countries was irregular, and this no doubt retarded the introduction of vaccination into France. The first French notice, in the form of a very concise statement, appeared in the *Bibliothèque brittannique* in October 1798. This was soon followed in the same journal by an almost complete translation of Jenner's "An Inquiry Into the Causes and Effects of the Variolae Vaccinae, a Disease Discovered in Some of the Western Counties of England, Particularly

Gloucestershire and Known by the Name of Cowpox." The first complete French translation, made in the winter of 1799-1800 by Count Joseph de la Roque, was published in Lyons, followed by two more editions within seven months. Also William Woodville's article (Reports of a Series of Inoculations for the Variolae Vaccinae or Cow-Pox, London, 1799) was now translated into French.

The Society of Medicine of Paris soon appointed the famous psychiatrist Pinel to investigate the matter, and the first vaccinations in Paris were done in August 1799 with virus received from Woodville. The first attempt was a failure. In January 1800 the medical faculty of the University of Paris and the National Institute appointed a committee to investigate, and Dr. Antoine Aubert went to London for this purpose; he became thoroughly convinced of the value of this practice and immediately sent some virus back to France; the virus was ineffective, and the attempt at vaccination again was a failure.

In the spring of 1800 La Rochefoucauld-Liancourt proposed the establishment of a vaccination institute similar to that founded by Pearson in London. As several persons in the French government were among the subscribers, soon the committee was offered a house and the Central Committee of Vaccination was organized. The war conditions made it difficult to obtain virus, but in June 1800 it was possible to vaccinate 30 children. As only 9 reacted satisfactorily and vaccination with virus from these 9 children was unsuccessful. the virus was considered to have degenerated, and the third attempt was a failure.

Now Dr. Woodville's offer to come to enemy France was accepted, but after being detained by all the red tape, his attempt at vaccination in Paris was a failure too. He had, however, vaccinated a few children at the time he landed in Boulogne, and these vaccinations were successful. With fresh vaccine from these children finally vaccination was permanently brought to Paris after four failures—lagging behind its introduction into Austria and Prussia (it had been introduced two months earlier into Geneva, which at that time was a part of France). By October the committee could report that 19 vaccinated children had been reinoculated with smallpox but that all were immune.

The progress was rapid. In 1801 a new building—this time in the center of Paris—was dedicated for the purpose of vaccination. Services were given free, and from here vaccine was distributed through the entire country. The final report of the Central Committee that Jenner was right was not made until 1803. Two other committees reported favorably on vaccination in 1801 and 1803 respectively.

Vaccination spread into the provinces of France from Paris and Geneva, and the author gives much information as to how it spread there during the following few years, and how quickly it became established with help from the Central Committee.

One reads with pleasure how it was possible—almost a century and a half ago—for a new medical procedure to be introduced into a country in the midst of war by an enemy doctor with the aid of an enemy land. The careful investigation by various committees before the method was adopted speaks well for the medical profession of the Napoleonic era.

ROSENTHAL, St. Paul.

POLIOMYELITIS VIRUS FROM FLIES. JOHN A. TOOMEY, WILLIAM S. TAKACS and LINDA A. TISCHER, Proc. Soc. Exper. Biol. & Med. **48**:637 (Dec.) 1941.

After many years of attempting to recover virus of poliomyelitis the authors succeeded in making a suspension from about 2,000 flies caught in fly traps placed near raw sewage. When this was injected intracerebrally and intraperitoneally and instilled into the nostrils of Macaca mulatta monkeys, poliomyelitis developed. A suspension of the cord produced poliomyelitis when injected into another monkey. A second isolation was made from flies collected in an outhouse.

HANSEN, Minneapolis.

TREATMENT OF EPIDEMIC MENINGITIS. ANTHON AANONSEN, Nord. med. (Med. Rev.) **12**:3659 (Dec. 20) 1941.

In 60 cases of meningococcic meningitis treatment was with sulfapyridine and specific serum, with rcovery in 56 cases.

WALLGREN, Göteborg, Sweden.

Acute Infectious Diseases

RHEUMATIC INFECTION IN CHILDHOOD: INFLUENCE OF TYPE OF ONSET AND CALENDAR YEAR OF ONSET. RACHEL ASH, Am. Heart J. **22**:439 (Oct.) 1941.

The course of 583 children who suffered from rheumatic infection during the years 1922 to 1936 is described. The average period of observation was nine and six tenths years. At the end of this time 64.2 per cent showed signs of heart disease and 21.7 per cent had died.

The mode of onset influenced the prognosis. Acute carditis presented the most serious prognosis; chorea, the most favorable prognosis.

A decrease in the severity of rheumatic infection was noted during the period of observation. The author believes that this trend toward a decrease in severity is due in part to a spontaneous change in the character of the disease and in part to more prolonged rest during the active phase of the disease.

GIBSON, Chicago.

STUDIES ON SULFADIAZINE: I. THE CHEMOTHERAPY OF EXPERIMENTAL HAEMOLYTIC STREPTOCOCCAL, PNEUMOCOCCAL AND STAPHYLOCOCCAL INFECTIONS IN MICE. PERRIN H. LONG, ELEANOR A. BLISS and EARL OTT, Bull. Johns Hopkins Hosp. **69**:297 (Oct.) 1941. II. THE CLINICAL USE OF SULFADIAZINE IN THE THERAPY OF BACTERIAL INFECTIONS, OTHER THAN PNEUMONIA. GORDON I. TREVETT, RUSSELL A. NELSON and PERRIN H. LONG, Bull. Johns Hopkins Hosp. **69**:303 (Oct.) 1941. III. THE USE OF SULFADIAZINE IN THE TREATMENT OF PNEUMOCOCCAL PNEUMONIA. F. T. BILLINGS and W. BARRY WOOD JR., Bull. Johns Hopkins Hosp. **69**:314 (Oct.) 1941.

In experiments on mice it was possible to produce and maintain high blood levels of sulfadiazine without injury to tissues. With equivalent blood concentrations in mice sulfadiazine was found to be as effective as sulfanilamide for streptococcic infections and as sulfathiazole for staphylococcic infections but less effective than sulfathiazole for pneumococcic infections.

Clinical experience with infections other than pneumonia make it appear that sulfadiazine is the best available drug for the treatment of chronic bacterial infections which require long periods of therapy. There was a relatively low incidence of toxic reactions. Clinical experience with sulfadiazine in pneumonia indicates that it is as effective as sulfapyridine and sulfathiazole. One of the factors which at present make it the drug of choice for pneumococcic infections is the preponderance of unconjugated sulfadiazine in the blood stream.

LYTTLE, New York.

CROSS INFECTION WITH TYPE I PNEUMOCOCCUS. SYDNEY S. GELLIS and A. GRAEME MITCHELL, J. A. M. A. **116**:2580 (June 7) 1941.

Nine cases are presented of children 2 and 3 years of age who contracted an infection with pneumococci of type I in a hospital. Most of them were convalescent from pneumonia or other illness in a ward where precautions were not carried out to prevent cross infections.

It is suggested that patients with pneumococcic infections be isolated during their whole stay in the hospital.

HEERSMA, Kalamazoo, Mich.

MULTIPLE INVASION OF THE BLOOD STREAM. ABRAM KANOF and BENJAMIN KRAMER, J. Lab. & Clin. Med. **27**:173 (Nov.) 1941.

In this paper are presented the cases of 24 children who had more than one organism in their blood stream. These mixed infections are classified as: (1) true mixed infections; (2) septicemia complicated by secondary bacteremia, and (3) spurious mixed septicemia.

In 9 of the cases the infection is classified as of the true mixed type, but in 6 of them the blood for culture was taken post mortem. Bacillus coli was a frequent organism in the true mixed infection.

In the second group there were 5 cases. In 3 of these the patients had septicemia due to Staphylococcus aureus and later hemolytic streptococcemia developed.

Ten cases of septicemia of the spurious mixed type were divided into two groups. In one the secondary invader was Streptococcus gamma or viridans, and in the second the organism was a variant of the primary invader.

GARD, Galveston, Texas.

RHEUMATISM IN CHILDHOOD AND ADOLESCENCE. P. KUTUMBIAH, Indian J. Pediat. **8**:203 (Oct.) 1941.

Rheumatism should be considered as a disease of the heart, with arthritis and chorea in the nature of complications. There is no satisfactory explanation of the increased vulnerability of the juvenile heart, but it is probably linked up with the greater vascularity of its valves. Vining believed that a nutritional defect, especially a vitamin B deficiency, prepares the soil for rheumatic infection. However, such failures of health are common to many diseases of childhood and may well be due to the rheumatic infection itself. While frank vitamin B deficiencies are fairly common in India, they do not occur at the age of susceptibility to rheumatism. It is probable that subclinical deficiencies of vitamin C are common in India as well as in western countries, but there is no proof of any relation to rheumatic infection. Tonsillar infection is believed to be extremely important, as only 1 of 457 patients

with rheumatic fever had had the tonsils removed prior to the initial infection. Of associated diseases, ankylostomiasis, congenital syphilis and herpes zoster were the most common. Arthritis either previously or on admission was found in 68 per cent. In order of frequency the joints affected were knees, ankles, hips, elbows, wrists, shoulders, great toe and neck. Rheumatic infection affects all structures of the heart but not to an equal degree. Acute, fatal pancarditis is rare in India. Mitral stenosis with regurgitation is the most common valvular lesion. Rheumatic nodules are rare. Chorea is said to be rare in India, but the author believes it is fairly common. Arrhythmias are uncommon. Pulmonary congestion, bronchopneumonia and pleurisy were found in several cases. Relapses occurred in 37 per cent. Sedimentation rates were regularly rapid. Nonhemolytic streptococci were found three times on culture of blood.

TENNEY, Madison, Wis.

ACTIVE IMMUNIZATION AGAINST TETANUS. D. G. EVANS, Lancet **2**:628 (Nov. 22) 1941.

Examination of the serums of 81 persons (aged 15 to 60 years) before active immunization against tetanus showed that none contained as much as 0.01 international unit of tetanus antitoxin per cubic centimeter.

Nine weeks after the first injection of tetanus toxoid the serums of 31 of 53 subjects showed antitoxin content of more than 0.01 unit but the serums of 22 still had less than this amount.

Seventeen weeks after the second injection of toxoid (given nine weeks after the first) 70 of 81 subjects had more than 0.01 unit of antitoxin, 68 more than 0.02, 59 more than 0.1 and 19 more than 1.0 unit.

The administration of a third dose of tetanus toxoid ten months after the second was followed by a large and rapid increase in antitoxin content of the serum, and the high level was maintained for a month.

LANGMANN, New York.

SEPSIS AND SEPSIS-LIKE DISEASE PICTURES. H. WISSLER, Ann. pædiat. **157**:198, 1941.

The symptoms arising from the mechanism of sepsis (bacterial spread from a septic source) are considered from the point of view of the "defense success." With complete failure sepsis acutissima, quickly proving fatal, develops; with relatively poor success, "classical sepsis" (otogenic sepsis, scarlet fever sepsis, etc.). Good defense success leads to illnesses which are not to be enumerated under sepsis. Some of these are well known and exactly defined: endocarditis lenta and the so-called "lenta form of meningococcic sepsis." In addition, there are a number of symptoms not yet classified, clinically resembling sepsis, which, however, take a favorable course and which show signs of hyperergic reactions (transitory exanthematic eruptions and eventually eosinophilia). These form the transition, on the one hand, to the so-called subseptic forms of chronic polyarthritis and, on the other, to symptoms having great similarity to rheumatismus verus. These should probably be considered the hyperergic reaction to a relatively slight bacterial spread.

AUTHOR'S SUMMARY.

Chronic Infectious Diseases

EFFECTS OF CONGENITAL SYPHILIS ON THE TEETH AND ASSOCIATED STRUCTURES IN CHILDREN. WILBUR D. JOHNSTON, BERT G. ANDERSON and PAUL F. MCALENNEY, Am. J. Orthodontics **27**:667 (Dec.) 1941.

Results are presented of a complete study of congenitally syphilitic children. A clinical and roentgenographic study was made plus a microscopic study of ground and serially sectioned teeth. Thirty-nine children were studied; plaster casts and roentgenograms were made of most of them.

The incisors, canines and first molars are involved as a group when congenital syphilis is present. Dwarfing of the entire tooth and lack of development of the premaxillary bone are consistent. Roentgenographic study revealed that the mandibular first molar was smaller than the mandibular second molar in 80 per cent of the teeth that could be measured. No unusual histologic changes could be attributed to congenital syphilis. The so-called Hutchinson triad was not observed in any patient. This, the authors believe, may be accounted for by early abortive treatment.

LEWIS, Dayton [ANGLE ORTHODONTIST].

CONGENITAL SYPHILIS IN A NEWLY-BORN BABY. Case Rep., Children's Mem. Hosp. **1**:3 (Feb.) 1942.

Clinical and pathologic observations on a 6 week old infant dying of congenital syphilis are presented. Treatment consisted of inunctions of preparations of mercury and administra-

tion of acetarsone. Discussion indicated that the methods of treatment rather than the drugs employed might have been responsible for the death.

DUSHANE, Evanston, Ill.

AGE INCIDENCE OF POSITIVE TUBERCULIN REACTIONS. FRANCES PASCHER and MARION B. SULZBERGER, J. Lab. & Clin. Med. **27**:332 (Dec.) 1941.

A random series of 362 persons were tested with tuberculin. In the entire series there were 248 positive reactions. The series is broken down into age groups, there being ten groups. The youngest group was 0 to 4 years and the oldest 60 to 80 years of age. In the 0 to 4 year group no positive reactions were noted. The highest percentage was in the 40 to 49 year group, with 98 per cent positive reactions. In this study the Mantoux test was used, and the doses were 0.02, 0.1 and 1.0 mg. There was a sharp rise in the incidence of positive reactions during the third decade, a rise from 33.3 to 90.9 per cent.

GARD, Galveston, Texas.

THE TUBERCULIN PATCH TEST. JOHN H. COLEBATCH, M. J. Australia **2**:640 (Dec. 6) 1941.

Tuberculin tests with Vollmer patches gave results that corresponded very closely with those of the Mantoux test. The notable discrepancies were those in children who had received intensive heliotherapy.

TENNEY, Madison, Wis.

THE PATCH TEST: A SIMPLE TUBERCULIN TEST FOR GENERAL MEDICAL PRACTICE. DOUGLAS ANDERSON, M. J. Australia **2**:645 (Dec. 6) 1941.

Storage of tuberculin patch test material in tropical climates sometimes results in inactivation of the material. A simple method of preparing the patches is described. Results obtained from patch tests were comparable to those obtained from the Mantoux tests.

TENNEY, Madison, Wis.

TUBERCULIN TESTS IN NEWBORN INFANTS VACCINATED WITH BCG. OLUF ANDERSEN, Nord. med. (Hospitalstid.) **12**:3553 (Dec. 13) 1941.

Newborn infants vaccinated with BCG often react only slightly when given a tuberculin patch test or an intracutaneous test. This is due to the fact that these children have only slight allergic reactions. In a study of 102 BCG-vaccinated infants it was shown that the children often react positively as soon as three weeks after vaccination and that the patch test is more sensitive than the intracutaneous test with 1 mg. of tuberculin.

WALLGREN, Göteborg, Sweden.

FLUCTUATIONS OF THE SENSITIVITY TO TUBERCULIN IN TUBERCULOUS CHILDREN DURING WHOOPING COUGH. S. T. HULTMAN, Nord. med. (Hygiea) **12**:3663 (Dec. 20) 1941.

Hultman presents a report of the results of repeated cutaneous tuberculin tests on 6 children with whooping cough. In 4 of them hypoergia was demonstrated during the first week following the catarrhal stage. Progression of the tuberculous process occurred in 2 of the children, and in 2 of them erythema nodosum developed, on the twenty-fourth and the thirty-third day of illness respectively.

WALLGREN, Göteborg, Sweden.

HYDRONEPHROSIS DUE TO INTRA-ABDOMINAL GLAND TUBERCULOSIS. SVEN HOLMGREN, Nord. med. (Hygiea) **12**:3741 (Dec. 27) 1941.

The author has collected 9 cases of hydronephrosis due to intra-abdominal gland tuberculosis from the medical literature and reports 2 hitherto unpublished cases of his own. One patient was a girl of 12 years and the other a man of 22. The lymphoma produced a dislocation and compression of the ureter, and thus a stenosis developed.

WALLGREN, Göteborg, Sweden.

Diseases of Blood, Heart and Blood Vessels and Spleen

STUDIES ON THE HEMORRHAGIC AGENT 3,3'-METHYLENEBIS (4-HYDROXYCOUMARIN): I. ITS EFFECT ON THE PROTHROMBIN AND COAGULATION TIME OF THE BLOOD OF DOGS AND HUMANS. JAMES B. BINGHAN, OVID O. MEYER and FREDERICK J. POHLE, Am. J. M. Sc. **202**:563 (Oct.) 1941.

The synthetic dicoumarin 3,3'-methylene-bis-(4-hydroxycoumarin) when administered orally or intravenously produced after a usual latent period of twenty-four hours or more prolongation of prothrombin time and coagulation time in dogs and human beings.

Therapeutic and fatal doses of this material given to dogs did not produce significant pathologic changes in the liver or other parenchymatous organs but did in many instances produce capillary, arteriolar and venular dilatations.

No harmful effects were observed from the administration of the dicoumarin to human beings.

The administration of synthetic vitamin K did not shorten the prothrombin time previously lengthened by administration of the dicoumarin, but transfusion of blood was temporarily effective in shortening the prothrombin time and coagulation time after they had been prolonged.

This dicoumarin may well prove to have an important place in clinical medicine as a substitute for heparin in the prevention and treatment of thrombosis and in the treatment of other conditions.

HENSKE, Omaha.

A CHILD WITH A SEVERE CONGENITAL HEART CONDITION SUCCUMBING TO INFLUENZAL MENINGITIS. Case Rep., Children's Mem. Hosp. **1**:8 (Jan.) 1942.

A case of fatal influenzal meningitis in a 22 month old infant with congenital heart disease (tetralogy of Fallot) is discussed, with particular emphasis on various aspects of treatment.

DUSHANE, Evanston, Ill.

SOME PROPERTIES OF HUMAN FETAL AND MATERNAL BLOOD. ROBERT C. DARLING, CLEMENT A. SMITH, ERLING ASMUSSEN and FELIX M. COHEN, J. Clin. Investigation **20**:739 (Nov.) 1941.

Data on the oxygen dissociation curves and on certain serum electrolytes of blood obtained from 13 pregnant and 6 nonpregnant women, and 8 human fetuses at term birth are reported. The fact that the dissociation curve of fetal bloods is displaced to the left compared with that of the bloods of women suggests the existence of a qualitatively distinctive fetal hemoglobin. The oxygen dissociation curve after birth shifts to the right, so that within thirty days it is like that of normal adult blood. The alkali reserve of fetal blood is markedly lowered; that of pregnant women, moderately so. This difference makes it probable that the difference in oxygen curves is less marked in vivo than at a constant p_H. The serums of the 2 premature infants, as well as those of 2 of the infants born at term, showed low values for sodium.

GUEST, Cincinnati.

THE MICROSEDIMENTATION RATE. ROBERT S. HERZOG, J. Lab. & Clin. Med. **27**:355 (Dec.) 1941.

Herzog reports his modification of the micromethod of Landau. The paper represents a study of 2,100 sedimentation rates obtained by this method. The author believes that the upper limit of normal with this method is 18 mm. per hour, with a mean of 8.5 mm. per hour. He describes in detail his method of using the Landau method of microsedimentation.

GARD, Galveston, Texas.

TECHNICAL FACTORS INFLUENCING THE WELTMANN SERUM COAGULATION REACTION. FRITZ B. SCHMEINBURG and LLOYD ROBERTS EVANS, J. Lab. & Clin. Med. **27**:366 (Dec.) 1941.

Certain possible causes of errors in the readings of the Weltmann reaction are brought out. The authors have reemphasized the importance of using the hexahydrate of calcium chloride. Also the importance of the p_H of the solution is mentioned and a graph is presented showing behavior of coagulation bands at different p_H values. The test should be read as soon as it is removed from the water bath. This avoids a false positive interpretation. It should be noted that serum tested need not be fresh if it is kept cold and sterile.

GARD, Galveston, Texas.

THE RELATIVE STABILITY AND POTENCY OF THROMBOPLASTINS FOR PROTHROMBIN TESTS. HENRY G. PONCHER, JEANNETTE RICEWASSER and KATSUJI KATO, J. Lab. & Clin. Med. **27**:385 (Dec.) 1941.

The authors present data obtained in fourteen series of observations. They compared the potency and stability of thromboplastin prepared by the technic of Quick and Magath. The rabbit brain powder prepared by the method of Quick demonstrated greater thromboplastic activity than the powder obtained by the method of Magath. If the preparation is stored in an air-tight bottle at 5 C., this superior potency of Quick's brain powder remains for a long

time—at least six months. Also it was noted that a suspension of rabbit brain powder, whether fresh or as old as six months, is still capable of yielding prothrombin clotting times comparable to those obtained with a fresh preparation. GARD, Galveston, Texas.

A CASE OF ACUTE HEMOLYTIC ANEMIA (LEDERER). KNUD HÖYER, Nord. med. (Hospitalstid.) **12**:3387 (Nov. 29) 1941.

A boy of 3 years had tonsillitis followed by fever, pallor, jaundice and hemoglobinuria. There was a severe anemia characterized by many anisocytes and numerous megaloblasts and normoblasts in the blood. The icteric index was increased; the osmotic resistance was normal, and the platelet count was reduced. Leukocytosis with numerous immature cells was observed. Transfusions of blood were followed by rapid recovery. WALLGREN, Göteborg, Sweden.

PHLEBOSTENOSIS SPLENICA. AXEL BOECK AUBERT, Nord. med. (Med. Rev.) **12**:3653 (Dec. 20) 1941.

A girl of 13 years during the last three years had suffered repeated attacks of hematemesis and melena. She had a posthemorrhagic anemia (hemoglobin content 26 per cent), leukopenia, splenomegalia and varices of the esophagus. Splenectomy was performed (weight of the spleen 500 Gm.), and an accessory spleen (10 Gm.) was also extirpated. Microscopically, there was venous hyperemia with hemorrhages. The girl was discharged healthy.

WALLGREN, Göteborg, Sweden.

Diseases of Nose, Throat and Ear

INDICATIONS FOR TONSILLECTOMY. GEORGE M. COATES and WILLIAM GORDON, Pennsylvania M. J. **45**:218 (Dec.) 1941.

The authors devote a considerable portion of their paper to a discussion of the "focus of infection, the anatomy, the function of the tonsil and the examination." They state that while a healthy tonsil has one or more functions in early life, an infected tonsil loses a large part of this function and may therefore actually encourage further local and systemic infection. It is admitted that in spite of a most careful examination of the tonsils, the examiner cannot be sure that infection is not present.

Indications for tonsillectomy are placed under these headings: (1) conditions within the tonsils; (2) conditions adjacent to the tonsils; (3) conditions remote from the tonsils.

In the first group are repeated attacks of tonsillitis, abscesses within the tonsils, epidemic streptococcic sore throat, tuberculous involvement of the tonsils, diphtheritic involvement of the tonsils (carriers), hypertrophy of the tonsils, Vincent's infection of the tonsils and halitosis due to tonsilar infection.

In the second group are acute catarrhal and suppurative otitis media, chronic suppurative otitis media (under certain conditions), middle ear deafness, labyrinthitis and middle ear deafness, sinusitis, thyroid disease, laryngitis, pharyngitis, cervical adenitis, peritonsillar abscess, ocular diseases and acute phlebitis and thrombophlebitis of vessels of the neck.

In the third group are listed a large number of remote systemic diseases which can result from tonsillar infection. WEINBURGER, Sayre, Pa. [ARCH. OTOLARYNG.].

RETROPHARYNGEAL ABSCESS. K. BREMER and H. C. WYKERD, South African M. J. **16**:41 (Jan. 24) 1942.

Retropharyngeal abscess is an uncommon but important condition because of its serious nature. The site of the abscess is the retropharyngeal glands, which undergo atrophy with advancing age; hence in most cases the lesion occurs in early childhood. It is usually due to acute infection of these glands, but there may be extension of tuberculous lesions of the neck. Diagnosis is made on a history of dyspnea—dysphagia, stridor and the palpation of a fluctuating mass in the pharynx. Treatment consists of administration of sulfonamide drugs and free incision of the abscess. Care must be exercised to prevent flooding the larynx with pus when the abscess is opened. TENNEY, Madison, Wis.

OTOLOGIC EXAMINATION OF 780 SCHOOL CHILDREN. W. SALEM, Arch. de pediat. **14**:27 (Dec.) 1941.

The author examined 780 school children between the ages of 5 and 12 years. He does not desire to present a catalogue-like list of otologic diseases but calls attention mainly to the correlation between the tonsils and adenoids (pharyngeal tonsils) and the ear. Of foci close

to the ear, the palatine and pharyngeal tonsils most frequently cause hearing deficiencies and disorders, such as otitis. Of course, the author himself states that this holds true only for chronic infections and does not take into account other etiologic factors, such as nervous, traumatic and toxic causes.

Although he found only 11 subjects with hypoacusia among all the children examined, 40 per cent had infected tonsils. The general organic repercussions of such a state are also studied. In all 11 cases of hypoacusia, the disorder was directly traceable to the tonsils.

SOTO, Habana, Cuba.

Diseases of Lungs, Pleura and Mediastinum

CHRONIC COUGH IN A NINE YEAR OLD GIRL. Case Rep., Children's Mem. Hosp. **1**:3 (Jan.) 1942.

A 9 year old girl with extensive bronchiectasis of the left lung died after a total left pneumonectomy. The cause of death was an embolus lodged in the basilar artery. The source of the embolus was the pulmonary vein in the stump of the removed lung. The cause and treatment of the bronchiectasis are discussed.

DUSHANE, Evanston, Ill.

CERVICAL MEDIASTINAL SEROUS CYST. A. CASTELLANOS and R. PEREIRAS, Bol. Soc. cubana de pediat. **13**:496 (Dec.) 1941.

The authors report an instance of this unusual condition in a Negro child aged 11 years. The cyst extended into the mediastinal space and seemed to involve the thymus.

The authors found the injection of a contrast medium, as advised by Castellanos, and a pneumomediastinal study valuable aids in the diagnosis of the case. The cyst involved chiefly the thymus. The fluid aspirated from it was replaced by a contrast medium, and roentgen studies revealed its full extent. It was removed surgically, with complete recovery of the patient.

SCHLUTZ, Chicago.

INFLUENCE OF CLIMATIC FACTORS ON BRONCHIAL ASTHMA. C. HULTING, Nord. med. (Hygiea) **12**:2979 (Oct. 18) 1941.

Hulting presents a report on observations during a four year period of the incidence of asthmatic attacks in 57 school children living in a home for children with asthma in Stockholm. There was no correlation between single climatic factors and the asthmatic attacks (the weather fronts were not studied). In 60 per cent of the cases the attacks could be traced to a preceding visit of the child to his own home and in 12 per cent to an intercurrent acute infection.

WALLGREN, Göteborg, Sweden.

EFFECT OF SOCIAL HYGIENIC MEASURES ON BRONCHIAL ASTHMA. B. NORDENFORS, Nord. med. (Hygiea) **12**:2982 (Oct. 18) 1941.

The role of sensitiveness to dust as a cause of asthma and the importance of eliminating this antigen in prevention of the attacks are emphasized. This prevention may be accomplished by removing the child from the dust-stricken dwelling or by removing the dust. Of 57 asthmatic children all but 3 reacted positively to a test with dust and were greatly improved when cared for in a dust-free environment.

WALLGREN, Göteborg, Sweden.

Diseases of the Gastrointestinal Tract, Liver and Peritoneum

FAMILIAL ACHOLURIC JAUNDICE ASSOCIATED WITH BONE CHANGES. ERIC L. COOPER, Ann. Int. Med. **15**:858 (Nov.) 1941.

The report deals with a family in which 10 members in three generations had congenital hemolytic anemia. Case reports of 3 members, aged 10, 11 and 14 years respectively, are given. Osseous changes as well as the mongoloid facies similar to that found in Mediterranean anemia were present in 1 of the reported cases.

READING, Galveston, Texas.

THE OPSONOCYTOPHAGIC TEST IN ACUTE DIARRHEA IN INFANTS AND CHILDREN. MERLIN L. COOPER and JANET P. MILLIKEN, J. Lab. & Clin. Med. **27**:347 (Dec.) 1941.

Though the opsonocytophagic test showed increased counts in patients infected with the dysentery bacilli, these tests did not furnish evidence suggesting any particular organism as an etiologic agent in children suffering from diarrhea with bacteria-free stools. It was found that

blood from patients infected with Shigella paradysenteriae but with no organisms in the stools also gave an increased index. It was felt the test helped in the diagnosis of infection with Shigella paradysenteriae, and a result below 0.5 probably meant the absence of a dysentery infection.

GARD, Galveston, Texas.

THE RESPONSE TO VITAMIN K: A LIVER FUNCTION TEST. ROBERT KARK and ALEXANDER W. SOUTER, Lancet **2**:693 (Dec. 6) 1941.

In patients with clinically evident disease of the liver five types of response to vitamin K therapy have been observed.

If the diagnosis is in doubt, rapid and complete return of a lowered blood prothrombin level to normal in patients with intense jaundice favors diagnosis of obstructive jaundice.

Failure of response to vitamin K when the blood prothrombin concentration is below 30 to 35 per cent of normal in patients with gross hepatic disease is indicative of advanced hepatic failure and is a grave prognostic sign.

In patients with other types of hepatic disease which respond incompletely or not at all to vitamin K, transfusion of fresh blood or fresh plasma is the only known therapeutic measure which can then increase the prothrombin concentration of the blood.

LANGMANN, New York.

DISCUSSION ON PYLORIC STENOSIS IN INFANCY. D. PATERSON, R. DOBBS, L. BARRINGTON-WARD and D. LEVI, Proc. Roy. Soc. Med. **35**:49 (Nov.) 1941.

Paterson states that the problem of medical as opposed to surgical treatment of pyloric stenosis should be examined (1) from the results obtained by each method and (2) from the availability of each method throughout the country. The results of medical and of surgical treatment are then discussed at length, and from the facts elicited the following conclusions are drawn:

1. Surgical intervention must still remain the method of choice for treatment in all but selected cases of congenital pyloric stenosis. This is particularly true in the case of very young infants who are progressively losing weight.

2. For patients seen after the eighth week who have made a slight gain and who have had good nursing, atropine methylnitrate should always be tried. The drug is best given in lamellas or in alcoholic solution in a concentrated form.

3. Better facilities for the isolation of infants from infection in the wards must be provided if the statistics of many of the Continental schools, especially in Scandinavia, are to be equaled. In the summary of Dobbs's discussion he states that medical treatment with atropine methylnitrate can be used with considerable success as a method of outpatient treatment. A considerable proportion of patients can be sent home within ten days, to return to the clinic weekly, and probably for those in whom dehydration and wasting are absent admission will in the future not be necessary. These are infants in whom symptoms appear late, probably after the fourth week of life; possibly girls respond more easily than boys. Of the rest, about half will be home within three weeks and the other half, more resistant, will need either prolonged medical treatment or operation. Whether operative or medical measures are undertaken in any given case depends among other things on surgical skill and the hospital and nursing facilities available, as well as on the age, sex and general condition of the patient. The question is not so much whether pyloric stenosis should be treated medically or surgically, but rather in which cases and under what circumstances medical treatment should be employed and when it should give place to surgical intervention.

Barrington-Ward points out that Rammstedt's operation has revolutionized the treatment for pyloric stenosis, and he also states that influence of segregation and avoidance of infection plays a great part in bringing about recovery. He feels that there is little choice between local and general anesthesia, but he prefers general. Drs. David Levi, C. Hardwick, W. Etherington-Wilson, Pearse Williams and Elaine Field also took part in the discussion.

WILLIAMSON, New Orleans.

TREATMENT OF CELIAC DISEASE WITH INTRAMUSCULAR INJECTIONS OF HUMAN BLOOD. J. WICKSTRÖM, Nord. med. (Finska läk.-sällsk. handl.) **12**:2889 (Oct. 11) 1941.

Wickström reports on 5 cases of celiac disease in small children treated with ten to thirty intramuscular injections of 15 to 20 cc. of whole human blood at two to five day intervals. The general condition, the appetite and the body weight greatly improved, while the character of the feces and the dextrose tolerance remained unchanged.

WALLGREN, Göteborg, Sweden.

ABSENCE OF CHRONIC IMPAIRMENT OF HEPATIC FUNCTION IN PERSONS WHO HAD HAD CATARRHAL JAUNDICE. CARL ROSENDAHL, Nord. med. (Med. Rev.) **12**:3091 (Nov. 1) 1941.

Ninety persons were examined one to forty-five years after the onset of catarrhal jaundice as to the functional capacity of the liver. There was no evidence of impaired function as compared with that of a group of healthy controls.

WALLGREN, Göteborg, Sweden.

CONGENITAL PYLORIC STENOSIS OF PROLONGED COURSE. ARVID WALLGREN, Svenska läk.-tidning. **38**:2874 (Dec. 24) 1941.

By roentgen examinations it has been shown that the muscular hypertrophy which produces the stenosis of the pyloric canal does not disappear concomitantly with recovery from clinical symptoms but may be demonstrated in decreasing degree during several years afterward. In general, the clinical symptoms disappear at the age of 3 months, sometimes a few months later. In rare instances the vomiting and the stenosis may continue unchanged until the child is 12 months old or more. A case in which there were clinical symptoms at the age of 9 months complicated with functional cardiospasm is reported by the author. At last the girl was discharged at 14 months of age, free from symptoms and in good health.

WALLGREN, Göteborg, Sweden.

Nervous Diseases

HUMAN INTELLIGENCE AFTER REMOVAL OF CEREBRAL TISSUE FROM THE RIGHT FRONTAL LOBE. D. O. HEBB, J. Gen. Psychol. **25**:257 (Oct.) 1941.

Hebb presents a report of 2 cases of surgical excision of scar tissue from the right frontal lobe. Intelligence tests before and after operation indicated that intelligence is not located in the frontal association areas.

WEINFELD, Highland Park, Ill.

A STUDY OF ERYTHROEDEMA POLYNEURITIS (PINK DISEASE). T. A. RATCLIFFE, J. Ment. Sc. **87**:545 (Oct.) 1941.

Ratcliffe reports 15 cases of pink disease, 6 of girls and 9 of boys. The author states that sex differences are probably of no etiologic significance. The age of onset varied from 3½ months to 1 year 5 months, and the mortality rate in his series was 13.3 per cent. It was impossible to trace a familial incidence. In many of the cases the onset of the disease appeared to be correlated with some other acute illness. Photophobia, anorexia, hypotonia and cutaneous rash were almost constant features, the rash being of less frequent occurrence than the others. Apart from hypotonia, neurologic symptoms were uncommon. In the patients personally examined by the author, the knee and biceps jerks were exceedingly difficult to elicit, but in no case were they absent. All of the bodily musculature was atonic, which may account for the sudden death from cardiac failure to which children with this disease are liable. Sensation was examined, so far as is possible in a baby, and there appeared to be diminution of sensibility for painful stimulation. The spinal fluid was examined in only 1 case and was found to be normal.

The psychologic state of the child is characterized by excessive irritability. For the most part the child lies curled up in the "knee-elbow" position, the face buried in the pillow. If disturbed, he will cry and withdraw from the examiner. Photophobia is usually noted. In a second type of the disease the child crawls about continually or rocks for hours or continuously performs acrobatic somersaults for a long time. In the rare type of the disease there is extreme lethargy, the child being miserable and irritable. This probably represents the advanced stage. No specific treatment for the disease is known, but particular attention is paid to dietetic measures.

It has been stated that the incidence of pink disease has been increasing in recent years, but this is probably more apparent than real. The question of etiology is still unanswered. One theory maintains the disease is due to a dietary deficiency, but the missing factor is unknown. It does not appear to be any of the known vitamins. A second theory postulates that the disease is caused by a specific organism or filtrable virus. No actual virus or organism has ever been isolated. Some attempts have been made to show that the disease is due to an endocrine disorder, but nothing definite is known about this factor. The prognosis should be guarded and the treatment directed toward combating the symptoms, particularly toward abolishing the irritability.

BRACELAND, Chicago [ARCH. NEUROL. & PSYCHIAT.].

THE ALLERGIC FACTOR IN IDIOPATHIC EPILEPSY. D. C. DEWAR, J. Ment. Sc. **87**:608 (Oct.) 1941.

Dewar reviews the subject of the possible association of epilepsy with food sensitization, starting with the work of Spratling, in 1904. His study of the literature suggested the

existence of considerable opportunity for further research. He examined three groups of patients, each group consisting of 24 persons. The first consisted of adults with idiopathic epilepsy. The second and third groups were picked at random from psychotic patients without epilepsy and the staff, respectively. The only common factor stressed was an approximation of the average age of the three groups.

The presence of allergic phenomena in the epileptic group was almost twice that of the other two classes combined. Actually, 66 per cent of the patients with epilepsy gave a personal or familial history of allergy. Each group was given cutaneous tests with group reagents and individual allergens. One week later the subjects were tested intradermally with a solution of proportionately modified strength. The final recording of positive results was based on intradermal responses irrespective of a corresponding negative or positive reaction to a scratch test. Fourteen epileptic patients gave positive reactions.

An interesting side light on the study is that the psychotic patients seemed to display a greater degree of allergic response than did the normal controls. The 14 epileptic patients were finally tested with individual allergens in an attempt to isolate the offending protein. The patients were then treated by means of intramuscular desensitization; after the fifth injection 2 patients, both sensitive to cheese, had fits; one of them died in what might have been coincidental status epilepticus.

The results of the desensitization of the remaining 12 epileptic patients is summarized as follows: (*a*) distinct improvement in incidence of fits and in the mental condition, 3 cases; (*b*) a lesser degree of improvement in incidence of fits and in the mental condition, 1 case; (*c*) improvement in incidence of fits alone, 3 cases; (*d*) improvement in the mental condition alone, 1 case; (*e*) no improvement, 3 cases; (*f*) death while under observation, 1 case.

The author concludes that his work confirms the postulated relation between allergy and epilepsy, the supporting facts being (1) the preponderance of allergic manifestations in the personal and family histories of the epileptic patients; (2) the greater sensitivity of the epileptic group to cutaneous tests; (3) the loss of diminution of cutaneous sensitivities following desensitization in all but 1 patient; (4) the association of sensitivity to a specific protein and seizures in the histories of 4 patients, and (5) the alleviation of symptoms by specifically directed treatment through elimination and desensitization in 9 patients.

BRACELAND, Chicago [ARCH. NEUROL. & PSYCHIAT.].

CUTANEOUS NAEVUS WITH BUPHTHALMOS AND EPILEPSY. REDVERS IRONSIDE and DENNIS HILL, J. Ment. Sc. **87**:631 (Oct.) 1941.

Ironside and Hill describe a case of Sturge's syndrome, so called because in 1879 Sturge gave the first complete account of a rare syndrome comprising the coexistence of naevus flammeus of the skin, glaucoma or buphthalmos and epilepsy.

The naevus flammeus appears characteristically over one side of the face within the distribution of the divisions of the trigeminal nerve. In the authors' case it extended over various segmental areas of the body. The buphthalmos or glaucoma occurs on the same side as the facial nevus. Within the cranial cavity two types of lesions have been described: (*a*) a venous cavernous angioma of the meninges and brain, sometimes penetrating as deep as the ventricular system, or (*b*) telangiectasis of the pia-arachnoid, with shrinkage and sclerosis of the underlying cortex and deposits of lime salts in the second and third cortical layers but not in the pial vessels. Weber added a fourth sign to the syndrome, the characteristic appearance of the roentgenograms of the skull.

The case described by the authors is that of a soldier with naevus flammeus and buphthalmos, who had repeated fits on the opposite side of the body while on duty with his unit. He was of low mentality but by no means mentally defective. Roentgenograms of his brain showed no calcification of the cerebral sulci. The contralateral fits which the patient described resembled migrainous attacks since they were preceded by teichopsia. The loss of consciousness and residual transient paresis of the left arm and leg, however, render it probable that he suffered from a type of jacksonian epilepsy, though no fit was actually witnessed in the hospital. In this patient no heredofamilial incidence of the syndrome in whole or part could be ascertained. The articles contains a good list of references on this unusual syndrome.

BRACELAND, Chicago [ARCH. NEUROL. & PSYCHIAT.].

FINGER TREMOR AND THE ALPHA WAVES OF THE ELECTROENCEPHALOGRAM. TORSTEN LINDQVIST, Acta med. Scandinav. **108**:580, 1941.

When one tries to keep a finger in a given position, slight oscillation occurs, which may be classified as tremor; its rate is 8 to 10 per second. Jasper, Gibbs and others thought this tremor to be caused by cortical function.

Lindqvist found that while under normal conditions the rate of alpha waves of the cortex and the finger tremor are frequently similar, under hyperventilation the rate of alpha waves slowed down but the frequency of tremor remained unchanged.

Two epileptic persons who had slow alpha waves had a normal rate of tremor.

These observations make it doubtful that the finger tremor is directly caused by changes in cortical potential.

KAJDI, Baltimore.

Psychology and Psychiatry

PSYCHIATRIC OBSERVATIONS OF CHILDREN WITH ABDOMINAL PAIN. JOHN P. LAMBERT, Am. J. Psychiat. **90**:451 (Nov.) 1941.

Twenty-five children were studied. They presented complaints of recurrent abdominal pain without organic evidence of abdominal disease. Three showed spastic colon on roentgen examination. Two girls had evidence of inactive rheumatic heart disease. One subsequently acquired Sydenham's chorea while under observation. Three showed epilepsy by the electroencephalogram. The intellectual capacity of these children ranged between 80 and 140 (intelligence quotient). Eating and sleeping habits were a prominent problem in all. All had worries of varying kinds and degrees. The parental attitude, the author believes, is the greatest factor in the problem. This is a good discussion and should be read in the original.

JAHR, Omaha.

THE ROLE OF DETECTIVE STORIES IN A CHILD ANALYSIS. EDITH BUXBAUM, Psychoanalyt. Quart. **10**:373, 1941.

Buxbaum reports the analysis of a 12 year old boy who was referred for treatment because of severe anxiety and inability to learn at school. The latter symptom was caused by the fact that he spent his entire time reading detective thrillers, which he felt under a compulsion to read. Analysis revealed that by this compulsion he could avoid feelings of anxiety. When he read the stories he made the detective his ego ideal whom he wanted to be like because his role was one which protected the victim of the crime and hindered the criminal. Unconsciously he identified himself with the victim of the story, who represented his passive wishes to be overcome and castrated. These wishes were frightening and were in conflict with his unconscious identification with the criminal, i. e., with his aggressive feelings against his sister, his mother and his uncle (his father was dead), which he feared lest they result in his castration.

PEARSON, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

ON THE POSSIBLE OCCURRENCE OF A DREAM IN AN EIGHT MONTH OLD INFANT. MILTON H. ERICKSON, Psychoanalyt. Quart. **102**:382, 1941.

Erickson reports the following observations on an infant which seemed to indicate that the child was dreaming. Her father was accustomed to play with her for a brief period each evening, just before she had her evening feeding. When she was exactly 8 months old he was absent from home on two successive nights. He returned in the evening after she was asleep and went into her room. Suddenly she started to go through the motions she made in her play, laughing as she did so. He left the room, and she did not awake. When she was 13 months old she started to laugh loudly in her sleep, which was so sound that even the changing of her diaper did not awaken her. When she was 23 months old her older sister fell and hurt her knee and the baby was much concerned. That night she started to cry in her sleep, saying "Carol [the older sister] bad bump." She was difficult to arouse, and when she awoke she seemed to be astonished that her sister was sleeping in the next bed.

PEARSON, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

JUVENILE DELINQUENCY IN WAR TIME. F. H. BODMAN and M. I. DUNSDON, Lancet **2**:572 (Nov. 8) 1941.

This report from the Bristol Child Guidance Clinic shows that there has been a 47 per cent general increase in the numbers of children referred from the juvenile courts in the war period 1940-1941 compared with 1939-1940 (when the war, as far as Great Britain was concerned, was still in a latent state). Among the mentally subnormal groups, the increase was disproportionately high, 74 per cent.

Whether the decrease of 23 per cent in the group of children with normal mentality indicated actually fewer offenses by this group or whether the apparent decline was merely the result of more opportunities to commit offenses with less chance of discovery it was impossible to determine.

The main rise in numbers was in the group of children classified as very dull. In this group (children with intelligence quotients of 70 to 80) the numbers rose sixfold. Added to the decrease of parental supervision there was also the effect of disorganization brought about in schools by damage, evacuation of personnel, altered hours of work and disturbed nights.

LANGMANN, New York.

TEMPERAMENT IN RELATION TO CONSTITUTION IN PERIODS OF GROWTH. P. MANFRINI, Med. ital. **21**:510 (Dec.) 1940.

This article must be read. It could not be easily abstracted. MARTOCCIO, Utica, N. Y.

Diseases of the Genitourinary Tract

THE CAUSE OF DEATH IN EXPERIMENTAL ANURIA. HEBBEL E. HOFF, PAUL K. SMITH and ALEXANDER W. WINKLER, J. Clin. Investigation **20**:607 (Nov.) 1941.

The concentration of potassium in the blood serum of animals rendered anuric increased regularly and progressively. This increase was thought to result from the breakdown of body tissues together with restricted ability to store potassium. In dogs rendered anuric by ureteral ligation or nephrectomy serum potassium increased until cardiac arrest occurred. Electrocardiographic evidence indicated that potassium poisoning was the effective cause of death in these animals. Dogs rendered anuric by injections of mercuric chloride usually died before the concentration of potassium in the blood serum rose sufficiently to cause cardiac arrest. Clinical observations were made on 5 patients with advanced chronic pyelonephritis and glomerulonephritis. In these patients the concentration of potassium in the serum was but little elevated, although the level of nonprotein nitrogen in the blood was extremely high, and the electrocardiograms showed no changes characteristic of potassium poisoning even just before death.

GUEST, Cincinnati.

CHEMILUMINESCENCE OF ALCAPTONURIC URINES. LYNN D. F. ABBOTT JR., Proc. Soc. Exper. Biol. & Med. **49**:14 (Jan.) 1942.

Alkaptone-containing urine obtained from 2 Negro children was found to emit a white glow when to 5 cc. of urine 1 cc. of 10 per cent solution of sodium hydroxide was added in a completely darkened room. The white glow is most intense on the second shaking and appears a fraction of a second after the shaking is stopped. The light fades rather rapidly, but there is an after-glow for some seconds after shaking. This can be repeated four or five times, and the intensity varies with the concentration of homogentisic acid (alkaptone). Lead homogentisate and homogentisic acid when added to normal urine produced a similar effect.

HANSEN, Minneapolis.

RENAL PHYSIOLOGY IN INFANTS AND CHILDREN: II. INULINE CLEARANCES IN NEWBORN INFANT WITH EXTROPHY OF BLADDER. HENRY L. BARNETT, ANNE M. PERLEY and HELEN G. MCGINNIS, Proc. Soc. Exper. Biol. & Med. **49**:90 (Jan.) 1942.

By catheterization of the ureters of a 24 hour old infant with extrophy of the bladder, urine was collected for six consecutive forty-five minute intervals after the administration of 10 per cent inulin in physiologic solution of sodium chloride intravenously. Inulin clearance of the infant was found to be considerably lower than that of adults. The inulin clearance varied directly with the minute volumes of urine.

HANSEN, Minneapolis.

NATURAL HISTORY OF BRIGHT'S DISEASE. ARTHUR ELLIS, Lancet **1**:72 (Jan. 17) 1942.

According to Ellis there are two varieties of nephritis differing in causation, mode of onset and course. Recovery is the rule in one and the exception in the other. Type 1 nephritis commonly has a history of preceding infection (84 per cent). Its onset is abrupt; blood is usually present in the urine, and complete recovery normally occurs (82 per cent). Type 2 nephritis has a history of preceding infection in less than 5 per cent of the cases, and even in these it is often indefinite. Its onset is insidious; blood is rarely present in the urine; the disease is progressive, and recovery is rare. Necrosis is included in type 2. The histologic picture in the two types is different, especially in the late stages.

Until further evidence is available, it is best to regard essential hypertension as nonrenal in origin.

So-called chronic interstitial nephritis is a hotchpotch of various renal disorders on which the vicious circle (renal ischemia → hypertension → lesions in kidney formerly regarded as "nephritis") has been superimposed.

LANGMANN, New York.

RENAL SPECIMENS. R. H. O. B. ROBINSON, Proc. Roy Soc. Med. **34**:769 (Oct.) 1941.

The author showed a renal tumor (Wilms) received from a male infant aged 15 months. There was a history of only three months' abdominal swelling. Roentgen treatment before operation had no effect on the tumor. Transperitoneal nephrectomy was performed, and six months later the child was apparently well. Macroscopically the tumor resembled a fibrosarcoma with a surprising amount of normal renal tissue present. Microscopically the appearances were typical of a Wilms tumor.

WILLIAMSON, New Orleans.

TUBERCULOUS ORCHIEPIDIDYMITIS IN AN INFANT OF TWELVE MONTHS WITH GENERALIZED TRACHEOBRONCHIAL GLANDULAR ENLARGEMENT. T. VALLEDOR, Bol. Soc. cubana de pediat. **13**:479 (Dec.) 1941.

The author reports the use of small daily doses of sulfanilamide (0.05 Gm. per kilogram of body weight in twenty-four hours).

In spite of very general miliary dissemination of the tuberculous process and massive tracheobronchial glandular involvement, the author was able to maintain the infant in fairly good condition for nearly a year before fatal termination with tuberculous meningitis. He points out that this condition, ordinarily rare at this age, usually terminates fatally within a few months, and he ascribes the long well-being of the infant to the use of the sulfonamide compounds.

SCHLUTZ, Chicago.

Diseases of the Ductless Glands; Endocrinology

CALCIUM APPETITE OF PARATHYROIDECTOMIZED RATS USED TO BIOASSAY SUBSTANCES WHICH AFFECT BLOOD CALCIUM. CURT P. RICHTER and JOHN R. BIRMINGHAM, Endocrinology **29**:655 (Nov.) 1941.

Parathyroidectomized rats kept on a low calcium diet but given access to calcium lactate solution showed a greatly increased appetite for calcium. This enabled them to survive without showing tetany.

Daily injections of parathyroid extract did not reduce the calcium appetite to its normal level until toxic doses were administered, but small doses of dihydrotachysterol and also of various concentrated vitamin D preparations (irradiated ergosterol, crystalline vitamin D_2, crystalline vitamin D_3, and irradiated cholesterol) were effective.

The effective dosages were found to be comparable to those used clinically, and it is therefore suggested that the appetite method may be used for the bioassay of substances which affect the calcium metabolism.

JACOBSEN, Buffalo.

GROWTH RESPONSE OF THYROIDECTOMIZED GOATS TO ARTIFICIALLY FORMED THYROPROTEIN. E. P. REINEKE and C. W. TURNER, Endocrinology **29**:667 (Nov.) 1941.

In young thyroidectomized goats the oral administration of an artificial thyroprotein produced by iodination of skim milk proteins arrests the development of cretinism and stimulates growth approaching that of the normal.

JACOBSEN, Buffalo.

EFFECT OF ADRENALECTOMY ON CARBOHYDRATE METABOLISM. GERALD EVANS, Endocrinology **29**:731 (Nov.) 1941.

In rats adrenalectomy results in an increased tendency to oxidize carbohydrate.

JACOBSEN, Buffalo.

STUDIES ON STILBESTROL: I. SOME EFFECTS OF CONTINUOUS INJECTIONS OF STILBESTROL IN THE ADULT FEMALE RAT. J. A. MORRELL and G. W. HART, Endocrinology **29**:796 (Nov.) 1941.

This work was undertaken to compare the effects of diethylstilbestrol (synthesized from anise aldehyde and identified by physical and chemical means as 4,4-dihydroxy-α,β-diethylstilbene) directly with those of natural estrogens (prepared from pregnant mares' urine) on the pituitary, thyroid, adrenals, pancreas, ovaries, uterus, vagina, liver and kidneys of animals treated with comparable estrogenic doses of both substances. There were no serious toxic effects and no essential differences in the reactions of the animals in the two groups.

JACOBSEN, Buffalo.

STUDIES ON STILBESTROL: II. EFFECT OF MASSIVE DOSES ON NORMAL IMMATURE FEMALE RATS. J. A. MORRELL and G. W. HART, Endocrinology **29**:809 (Nov.) 1941.

In immature female rats the changes in the endocrine glands following treatment with diethylstilbestrol were characteristic of the effects of estrogenic treatment. Even with the large doses employed no definite evidence of toxicity of diethylstilbestrol was obtaind.

JACOBSEN, Buffalo.

EFFECT OF SEX AND GONADOTROPIC HORMONES UPON THE BLOOD PICTURE OF THE RAT. ERWIN P. VOLLMER and ALBERT S. GORDON, Endocrinology **29**:828 (Nov.) 1941.

Various androgens are shown to affect the erythropoietic activities of the bone marrow of hypophysectomized animals. It is suggested that the anemia following hypophysectomy is due in part to a disturbance in metabolism resulting from atrophy of various endocrine glands and that the gonadal secretions are responsible for the sex difference in the normal erythrocyte count encountered in many species of animals.

JACOBSEN, Buffalo.

HYPOPHYSIAL SYNDROME AND DIABETES. DE LA B. FORTIER, Union méd. du Canada **70**:1305 (Dec.) 1941.

A girl of 11 years 10 months had been treated for diabetes since she was 1 year old. She was 42 inches (107 cm.) tall and weighed 54 pounds (24.5 Kg.). Her chest and abdomen measured 25½ and 27½ inches (65 and 70 cm.) respectively. Her legs were only 19 inches (48.3 cm.) long, and her head was 19 inches in circumference. Her diabetes was not controlled satisfactorily during a month of hospitalization, and the author concluded that a hypophysial syndrome with sexual infantilism must be present. A course of treatment with a gonadotropic substance was begun, but her stay in the hospital was too short to permit an evaluation of results. However, the use of 300 units daily, without any insulin, lowered the values for blood sugar from 290 to 230 mg. per hundred cubic centimeters. Roentgenograms showed the sella turcica to be of normal size, while her carpal bones were at the level of development of 5 to 7 years.

DAFFINEE, Boston.

HYPOTHYROIDISM IN THE GENESIS OF URINARY AND FECAL INCONTINENCE. EUGENIO CIENFUEGOS, Arch. de pediat. **14**:7 (Nov.) 1941.

In a physiopathologic discussion supplemented by reports of cases the author ably covers the subject; methods of treatment and the results obtained are set forth in each case presented. The author reaches the following conclusions:

1. Hypothyroidism should be taken into account in the pathogenesis of urinary incontinence.

2. A high percentage (50 to 60 per cent) of children with this disability are cured with thyroid therapy.

3. In cases in which fecal and urinary incontinence are not due to a perament organic lesion, thyroid therapy may be the elective treatment.

4. Syphilis may be an etiologic factor, and its treatment should be essayed jointly with thyroid therapy.

5. In any case, thyroid therapy should be the first treatment attempted for children with incontinence of urine or of feces.

SOTO, Habana, Cuba.

DOES SO-CALLED FREE DIET PRODUCE PRECOCIOUS ARTERIOSCLEROSIS IN DIABETIC CHILDREN? FRITZ KARLSTRÖM, Svenska läk.-tidning. **38**:2623 (Dec. 5) 1941.

Karlström presents studies of the cholesterol content of the plasma of electrocardiograms of blood pressure readings and of examinations of the eyes of 38 diabetic children given a free diet. A correlation was found between the need of insulin and the cholesterol content of the plasma, but the degree of hyperglycemia did not influence the content of cholesterol. Seven of the children showed abnormal electrocardiograms, the cause of which could be detected for 5. The average blood pressure was somewhat higher than normal (ambulatory readings). In no case could a cataract be demonstrated. The author concludes that no finding favors the hypothesis that diabetic children on a free diet have a more precocious and pronounced arteriosclerosis than other patients with diabetes.

WALLGREN, Göteborg, Sweden.

DOES THE FREE DIET PRODUCE PRECOCIOUS ARTERIOSCLEROSIS IN DIABETIC PATIENTS? N. E. LUNDBERG, Svenska läk.-tidning. **38**:2808 (Dec. 19) 1941.

This is a criticism of the article of Karlström with the same title (*Svenska läk.-tidning.* **38**:2623 [Dec. 5] 1941). The influence of free diet as compared with restricted diet cannot be judged until several decades have passed since the beginning of this treatment. At present nothing can be said about the tendency of the free diet to produce an early arteriosclerosis.

WALLGREN, Göteborg, Sweden.

Diseases of the Muscles, Bones, Joints and Lymph Glands

FURTHER EXPERIENCE WITH THE USE OF GUANIDINE HYDROCHLORIDE IN THE TREATMENT OF MYASTHENIA GRAVIS. KATHRINE DODD, S. S. RIVEN and A. S. MINOT, Am. J. M. Sc. **202**:702 (Nov.) 1941.

Guanidine hydrochloride causes temporary improvement in muscular function in most patients with myasthenia gravis. Persons with this disease have an increased tolerance of guanidine. Prolonged medication produces sustained improvement in muscular function without harmful effects. As a rule, less of the drug is required after several months of adequate medication. Individual attention is necessary to establish a proper schedule of medication, but frequent readjustment of the guanidine ration is thereafter unnecessary. Guanidine, unlike prostigmine, does not inhibit the activity of choline esterase. It may play a fundamental role in restoring irritability to cells.

HENSKE, Omaha.

ROENTGENOLOGIC CHANGES IN THE BONES IN CASES OF PSEUDOHYPERTROPHIC MUSCULAR DYSTROPHY. BERNARD S. EPSTEIN and JOSEPH L. ABRAMSON, Arch. Neurol. & Psychiat. **46**:868 (Nov.) 1941.

The authors report a series of cases of muscular dystrophy with involvement of the long bones and pelvic bones. The condition is more generalized than has been supposed. It is now recognized as involving the muscular system, the creatinine and carbohydrate metabolism and possibly the endocrine glands and the bones.

BEVERLY, Chicago.

EPIDEMIC MYOSITIS WITH NEURITIS, ERYTHEMA AND MENINGEAL SYMPTOMS. DENIS WILLIAMS, Quart. J. Med. **10**:283 (Oct.) 1941.

Five cases of an unusual syndrome occurred at a Royal Air Force station during the summer of 1940. The patients were 23, 26, 20, 21 and 20 years of age respectively, and all were healthy recruits.

The illness in each case began within forty-eight hours of inoculation with T. A. B. vaccine (a typhoid and paratyphoid A and B vaccine). The onset was acutely febrile, with signs of meningitis, myositis and cutaneous eruptions. The spinal fluid was sterile and contained excess of cells in 3 instances. Attempts to isolate a filtrable agent were not made.

The relationship of the symptoms to those of allied diseases is discussed by the authors.

BRADFORD, Rochester, N. Y.

Diseases of the Eye

ORTHOPTIC TRAINING AND THE SURGICAL CORRECTION OF STRABISMUS. C. BERENS, A. J. ELLIOT and L. SOBACKE, Am. J. Ophth. **24**:1418 (Dec.) 1941.

From an analysis of the histories of 324 patients with strabismus operated on at the New York Eye and Ear Infirmary, Berens, Elliot and Sobacke conclude that orthoptic training is an indispensable adjunct to the surgical treatment of strabismus.

W. S. REESE [ARCH. OPHTH.].

OPHTHALMIC ASPECTS OF ACUTE OXYGEN DEFICIENCY. R. A. MCFARLAND, J. N. EVANS and M. H. HALPERIN, Arch. Ophth. **26**:886 (Nov.) 1941.

The human eye may manifest marked alteration in any of its functions when the supply of oxygen is inadequate. The brain is most sensitive to anoxia, especially the cerebral cortex. Irreversible changes are found in the cortical tissue if it is deprived of oxygen for more than five to eight minutes, as compared with other parts of the brain and spinal cord, in which irreversible changes do not occur when anoxia is continued for as long as twenty to thirty minutes. This is in contrast to the survival time for smooth muscle tissue, for instance, which may be hours. Since the retina is essentially an extension of the brain and

resembles it both histologically and functionally, one might expect the retina to be especially sensitive to oxygen deprivation.

The authors' investigations were based on a study of the following functions: (*a*) visual sensitivity, including light sense and dark adaptation; (*b*) differential sensitivity of visual intensity; (*c*) visual, that is foveal, acuity; (*d*) peripheral and central visual fields; (*e*) color vision; (*f*) after-images; (*g*) flicker fusion frequency; (*h*) intraocular tension; (*i*) extraocular muscle balance; (*j*) accommodation and convergence, and (*k*) coordinated ocular movements.

Their observations may be tabulated as follows:

The minimum, absolute threshold for light is impaired. Dark adaptation is impaired.

Visual acuity (foveal) is decreased in dim light but is practically unaffected in bright light.

The central visual fields are decreased by widening of the angioscotoma.

Color vision is apparently further impaired if it is abnormal prior to anoxia.

The latent period of the after-image is prolonged.

The diameters of the arteries and of the veins in the fundi are increased about one eighth.

Weaknesses of the extravascular muscles become significantly exaggerated.

The range of accommodation is decreased.

The ocular motor reactions, such as those employed in reading, are less orderly, and latent defects become apparent.

There is a diminished precision in fixating on test objects, and motor anomalies become accentuated.

SPAETH, Philadelphia [ARCH. NEUROL. & PSYCHIAT.].

RETINITIS PIGMENTOSA WITH MACULAR DYSTROPHY: REPORT OF A FAMILIAL GROUP. A. SORSBY, Brit. J. Ophth. **25**:524 (Nov.) 1941.

Sorsby previously reported a case of pigmentary degeneration of the retina with macular dystrophy. In this particular case no hereditary or familial incidence could be established; so there was some lack of validity in drawing on the case for an argument in favor of clearly defined familial and hereditary lesions. The present note supplies the necessary validity, as it concerns a familial group showing the association of the two lesions. Two of the four sons and one of the two daughters were affected. The father was a cousin of the maternal grandfather.

Ophthalmoscopically the two parents showed essentially the same picture. Typical bone corpuscle pigment was distributed rather unevenly over the different sectors of the fundi, which also showed gross pigmentation here and there. The disks and retinal arteries were characteristic of retinitis pigmentosa, and there was considerable unmasking of the choroidal circulation. The macular lesions were of the dystrophic type.

This group may be taken as lending support to the view that macular dystrophy cannot be put in sharp antithesis to generalized retinal dystrophy, of which retinitis pigmentosa is the best known type. The various clinical types of retinal dystrophy are not rigid entities but probably localized expressions of one fundamental disturbance.

The article is illustrated.

W. ZENTMAYER [ARCH. OPHTH.].

Skin Diseases; Allergy

POWDERY MILDEWS AS ALLERGENS. VERNON G. ALDERSON and LUCILLE R. MASON, California & West. Med. **55**:241 (Nov.) 1941.

During a routine study of pollen slides, an unknown type of spore was found to occur in great numbers. Study disclosed the source of these spores to be a powdery mildew, Microsphaera alni, growing on the leaves of the valley oak. In view of the seasonal occurrence of these spores, 100 subjects were tested with an extract prepared from them; persons chosen as subjects were those showing seasonal symptoms and known to be sensitive to pollen. In 65 per cent of these cases reactions from 1 to 4 plus were obtained; only 10 per cent of the control group showed some reaction.

The spores of these fungi may be the cause of many of the baffling and unexplained allergic reactions. The millions of readily dispersible conidiospores produced by a single infection and the great abundance of the fungi of this group on a wide variety of hosts render these plants ideal as a causative agent of asthma and hay fever.

DAVIS, San Francisco.

SEROLOGIC CHANGES AFTER ORAL RAGWEED POLLEN THERAPY IN CHILDREN. SAMUEL J. LEVIN and LILLIAN SHULSKY, J. Allergy **13**:1 (Nov.) 1941.

The purpose of the work was to determine whether ingested pollen is absorbed in sufficient quantities to effect serologic changes approximating those occurring in hypodermically treated patients. Thirteen children were treated hypodermically, and 10 were treated orally. Those treated hypodermically received from 5,000 to 27,000 Noon pollen units, while those treated orally received up to 2 grains (0.13 Gm.) of ragweed pollen (240,000 Noon pollen units) a day. The neutralizing and skin-sensitizing capacity of the serum was increased in both instances, which indicates that ragweed pollen is absorbed from the intestinal tract.

HOYER, Cincinnati.

A CLINICAL STUDY OF HISTAMINE AZOPROTEIN IN ALLERGIC DISEASE: A PRELIMINARY REPORT. J. M. SHELDON, N. FELL, J. H. JOHNSTON and H. A. HOWES, J. Allergy **13**: 18 (Nov.) 1941.

Histamine azoprotein (histamine azo despeciated horse serum globulin) was used in treatment of a group of patients with various allergic conditions. The number of cases studied was small. The best results were obtained in physical allergy and in cutaneous hypersensitivity. The authors feel that their results warrant further study.

HOYER, Cincinnati.

THE APPEARANCE OF POLLEN IN THE STOOL. E. L. MACQUIDDY, J. Allergy **13**:41 (Nov.) 1941.

Ragweed pollen was found in the stools of normal persons as well as in those of allergic patients. The question arises as to whether some of the symptoms in hay fever may be caused by the swallowed pollen.

HOYER, Cincinnati.

THE SPEED OF ACTION OF SO-CALLED "SLOW EPINEPHRINE" (IN OIL). L. C. BACON, M. STICKLER and R. W. LAMSON, J. Allergy **13**:48 (Nov.) 1941.

Thirty-six ambulatory asthmatic patients were studied. Their symptoms were so severe that they did not respond to the usual remedies. The study was undertaken to rule out the possible psychic factors that enter into judging the efficacy of a preparation. The authors believe from their evidence that epinephrine base in oil is not slow in its action; that small doses frequently are effective, and that the time between its administration and its pharmacologic effect compares favorably with that for equivalent doses of an aqueous preparation of an epinephrine salt.

HOYER, Cincinnati.

PAPULONECROTIC TUBERCULOSIS IN CHILDHOOD. T. VALLEDOR, Bol. Soc. cubana de pediat. **13**:460 (Nov.) 1941.

The patients were 2, 4 and 7 years of age, respectively. They showed tuberculous lesions which became necrotic. The author believes the lesions represent a hyperallergic state brought about by an intensely positive reaction to a Mantoux test.

One of the children showed considerable perifocal pulmonary involvement; another showed a serofibrous pleuritic exudate; the third showed miliary dissemination and a positive reaction to tuberculin.

SCHLUTZ, Chicago.

Society Transactions

CHICAGO PEDIATRIC SOCIETY AND CHILDREN'S DIVISION OF COOK COUNTY HOSPITAL

JESSE R. GERSTLEY, M.D., *President*

Joint Meeting, Dec. 15, 1942

Bacillus Coli Peritonitis and Meningitis in a Newborn Infant. ARTHUR H. PARMELEE, M.D.

On Sept. 30, 1942, a Negro infant was born in Cook County Hospital; it was examined in the first twenty-four hours of life and was pronounced normal. On the sixth day the temperature suddenly rose to 102 F.; examination at that time gave no clue to the cause. The child was breast fed; it nursed well and had not lost weight, being only 4 ounces (113 Gm.) under the birth weight of 6 pounds 11 ounces (3,033 Gm.). During the next few days the elevation of temperature continued. Repeated examinations showed no bulging of the fontanel and no neurologic symptoms but some distention of the abdomen. The urine was normal; the leukocyte count was 11,800, with fairly normal distribution of cells. About the eighth day it was noted that the child tended to assume a somewhat opisthotonoid position. The fontanel was sunken rather than bulging. A spinal tap was performed, and the count showed 16,000 leukocytes; the smear did not show any organisms. The culture yielded a pure culture of Bacillus coli.

Use of sulfadiazine was ordered, and the temperature came down rather promptly. Dr. Levinson saw the baby on the fourteenth day of life, after sulfadiazine had been given for four days, and noted no signs of meningitis. Progress was satisfactory, and on October 24 the child was about to be discharged from the hospital when the temperature rose to 103 F. and vomiting occurred. Symptoms of partial obstruction were evident, and a roentgenogram taken on October 27 showed definite obstruction of the ileum. Dr. Edwin M. Miller performed an operation on October 28 and on opening the abdomen found that all the loops of bowel were tightly bound down by adhesions from old peritonitis. He performed a lateral anastomosis between the loops of bowel at the point where it seemed most constricted. After a stormy period, convalescence was normal until November 22, when the child was 54 days old. It was noted at 9:30 that the baby was resting and comfortable; at 9:50 the baby was dead.

The autopsy revealed anemia of the myocardium, chronic fibrinous peritonitis and chronic focal meningitis. Culture from the brain and from the spleen yielded B. coli.

B. coli meningitis is encountered only in newborn and in very young infants. Cases of recovery have been reported, but practically all infants who have it die. The etiology has not been adequately explained. Was the peritonitis primary and the meningitis secondary, or were both part of the B. coli sepsis? The mother was not ill before or during labor and showed no signs of illness afterward. There was no evidence of anything wrong with the placenta or amniotic fluid. The child was breast fed, and there was no possibility of contamination except from the mother.

Chronic Stomatitis of Unknown Cause. M. P. BOROVSKY, M.D.

This child, aged 2 years, has been under observation in the hospital for nine months. We have had the advice of many pediatricians, oral surgeons, dermatologists, dentists and neurologists, and have used practically every form of therapy. When she came to the hospital, there was a history of a cough, apparently pertussis, about six weeks before. She had ptyalism for about two weeks and sores about the mouth for about a month. She had been taking orange juice prior to the time when she complained of its burning the mouth.

There is profuse salivation, and red crusted areas are present about the mouth. The tissue is edematous and bleeds easily; the gums bleed easily. On the mucous membrane of the mouth are scattered white areas, slightly elevated, and superficial ulceration. At this time the scalp is clean except for a few papules.

For several days following any new therapy there seems to be improvement; then retrogression. Five per cent solution of chromium trioxide, sodium perborate for a mouth wash; vitamin C, brewers' yeast and cod liver oil have all been tried. Sulfathiazole ointment was used on the neck; some improvement followed, and then the condition became static. Gentian violet was tried, with some improvement temporarily and then retrogression to a condition somewhat worse than the previous state. Large doses of vitamin B were given parenterally without effect. Tincture of benzoin locally gave no benefit. Sulfathiazole was given by mouth and in lozenges, without effect. The child had become dehydrated and anemic, and several blood transfusions were given and fluids were administered intravenously.

About a month after her admission to the hospital the lesions on the scalp looked like typical pyoderma, with pustules occurring all the way down the neck and down the back. Some secondary paronychia developed.

At this time a new course of therapy was instituted; ammoniated mercury ointment was applied, and then potassium permanganate wet dressings and ammoniated mercury ointment. Acetarsone was given until it was thought the patient was showing signs of arsenic intoxication. On the theory that there might be a blood dyscrasia, sternal puncture was done, but nothing significant was found. With a substantial dose of nicotinic acid, a blotchy generalized eruption developed; no therapeutic effect was noted. Intravenous injection of typhoid vaccine elevated the temperature to 104.5 F. without benefit. Ultraviolet irradiation was used for a considerable time, without benefit. Local applications of diethylstilbestrol ointment produced no effect.

Since the lesions followed pertussis, it was thought that it might be well to desensitize her by small increasing doses of pertussis vaccine; no improvement resulted. Potassium iodide was given without benefit. Penicillin locally did not show a beneficial effect. Yeast paste was also valueless.

The condition is about the same as it was nine months ago except that the neck and scalp are worse. The only positive finding has been the obtaining of a yeast on culture of material from the lesions of the mouth, and these lesions have not responded to the usual therapeutic aids against yeast infection.

DISCUSSION

DR. MINNIE PERLSTEIN: I suggest a diagnosis of dermatitis herpetiformis (Duhring's disease), because of the grouped lesions all over the back, the upper part of the neck and the mouth, which are compatible with those seen in that disease. They are herpetic, varying from simple vesicles to hemorrhagic lesions. They run a course and undergo involution with periods of remission and exacerbation. The percentage of eosinophils in this child's blood varies from 16 to 59. This is high enough for a diagnosis of Duhring's disease. Therapy for this condition was unsatisfactory until about six months ago; since then dermatologists have been using sulfapyridine with good therapeutic results. We have given 1 child small doses for four months; there have been no toxic symptoms, and her cutaneous lesions have been alleviated. That child had had Duhring's disease for four years without any improvement in spite of all previous treatment.

DR. M. P. BOROVSKY: Other dermatologists have seen this child but have not made such a suggestion. We shall be happy to try it. I should say the patient has hypervitaminosis rather than hypovitaminosis. We have not noted any aggravation of the lesions with potassium iodide; a 75 minim (4.6 cc.) dose was given without any effect.

DR. MINNIE PERLSTEIN: A type of oral lesion is encountered in periadenitis mucosa necrotica recurrens, but the ulceration is extremely deep. There have been instances in which allergy has been thought to be the etiologic factor. The cause of dermatitis herpetiformis is not known. This child impresses me as a patient with dermatitis herpetiformis with a severe superimposed vitamin B deficiency.

Lead Poisoning in Two Sets of Twins. MEYER A. PERLSTEIN, M.D.

Although lead poisoning in children is not infrequent, its occurrence in twins is not common. I am showing two sets of twins, two white boys seen in private practice and a Negro boy and girl seen in the clinic, to show that the condition is no respecter of race or creed or economic status.

These twin white boys are just over 3 years of age. Only 1 of these children had lead intoxication, the other being symptom free. The sick one was a child who sucked everything he got hold of—toys, lead soldiers, dirt and, in fact, anything. The source of lead was a set of lead toy soldiers and automobiles. He had convulsions, coma and fever as his initial symptoms. On admission to the hospital he had symptoms of acute intracranial hypertension.

The diagnosis was suggested by the roentgenogram, which showed a thickened epiphysial line suggestive of lead poisoning. There was also 6 per cent basophilic stippling of the red blood cells. The diagnosis was corroborated by finding an increased content of lead in the blood and urine. With symptomatic and specific treatment with phosphates, the boy has made a complete recovery.

This Negro girl was also seen in coma, with convulsions, vomiting and fever. She had been in the hospital about a month before with convulsions, at which time the diagnosis was not made. At the last admission, the lead line in the bones and the basophilic stippling were noted. The diagnosis was corroborated by finding a pronounced elevation in the lead level of the blood. She has not made a complete recovery. She has the appearance of decerebrate rigidity and simply vegetates. The toxic effect of the lead has resulted in severe atrophy of the cortex, which has been demonstrated by pneumoencephalography. Apparently she is blind. There is no evidence yet of atrophy of the optic nerve, but it will probably develop within the next few months.

The twin brother of this girl, although symptom free, has basophilic stippling of the red blood cells, a lead line in the bones and an elevated content of lead in the blood. The source of lead in these cases was the drinking water, which ran through lead pipes.

Most cases of lead encephalopathy we have observed have been due to burning of battery casings, from which the lead is volatilized. The old time lead nipple shields, which formerly were a common cause of lead poisoning, are now rarely used in the United States. Lead toys, paint, metal dishes and gasoline are other sources of lead intoxication.

Although calcium given parenterally will give relief from lead colic, it is not always a cure. We rather lean toward the treatment advocated by Shelling, of giving phosphate in the hope of depositing the lead into the bones or of having it excreted as an insoluble salt. For this purpose sodium biphosphate is given. We also give phosphorized cod liver oil. During the acute stage of the encephalopathy, treatment is directed toward reducing intracranial tension and checking convulsions. Death is not uncommon from lead intoxication. Sequelae, such as convulsions, mental deterioration and blindness, are more common than is generally supposed.

DISCUSSION

DR. I. M. LEVIN: How often have any of you seen bismuth poisoning in children who are under antisyphilitic treatment with bismuth? I have repeatedly looked for bismuth lines in the gums and for other signs of intoxication in children who are receiving large doses of the substance, but I have not been able to demonstrate bismuth lines in the bones.

DR. MEYER PERLSTEIN: Many years ago I saw some children with tuberculous sinuses, in whom bismuth poisoning developed from treatment with a paste of bismuth subnitrate in petrolatum (Beck's paste). There were lines in the gum that looked like those encountered in adults with lead poisoning. It should be remembered, however, that lead lines in the gums are rare in children with plumbism.

DR. A. H. PARMELEE: The lead line in the bones is more intense in lead poisoning. Christy found heavy transverse lines at birth in a baby whose mother had had bismuth during pregnancy.

DR. I. M. LEVIN: In contrast with lead poisoning, in bismuth poisoning there is no bismuth in the bones.

DR. J. K. CALVIN: All heavy metals that interfere with resorption will cause this white line; phosphorus will also cause a heavy line in the bones.

DR. P. L. ARIES: In a series of mothers who had massive doses of bismuth during pregnancy we found no such lines.

DR. M. L. BLATT: I am sure that lead poisoning does occur from burning battery boxes, but the method of production has always been a question to me. Lead does not distil off at low temperature; I think it must be heated to 2,000 F.

DR. MEYER PERLSTEIN: Exposure over a long period seems to be the factor. The rate of volatilization is apparently high enough in an ordinary stove to reach a dangerous level. We had 1 case in which the poisoning was caused by ordinary flashlight batteries burned in the stove. There must be some factor other than lead responsible for the formation of the lead line in bone, possibly the combination with phosphorus. Our patient with the worst lead poisoning and the highest blood level of lead had no lead line.

Sickle Cell Anemia in a Newborn Infant. I. PAT BRONSTEIN, M.D.

This child was born on July 25, 1942 and was brought to the hospital on August 5 because of umbilical bleeding. The icteric index was 200. At the age of 1 month, jaundice increased

and the index rose to 421; the urine was bile stained. The possibility of an anomaly of the biliary passages was considered. About two weeks later the icteric index fell to 107; the jaundice, however, had increased, and the liver was palpable. There was striking diminution of the cholesterol esters. The red blood cell count rose to 5,000,000, and the impression of anomaly of the biliary passages was questioned.

During the next few weeks the icteric index rose to 222, and surgical intervention was again considered. Then the index fell to 100 and then to 63. The child lost weight and seemed to be losing ground. At the end of two months, while surgical treatment was still being considered, sickling was found in the blood, and this eliminated a laparotomy. At the age of 3 months some distention of the abdomen developed; this cleared up. At 4 months there was an infection of the upper respiratory tract, and the child is not doing very well. The cause is, of course, obscure. There have been cases in which extremely active sickling has become latent; but the earlier the age at which it occurs, the less favorable the prognosis.

Malrotation of Bowel with Obstruction. BERNARD GUMBINER, M.D.

This baby was admitted to the hospital seven days after birth with a history of apparently normal progress until the fifth day of life, when vomiting of all feedings started. The vomiting was forceful, and the vomitus was bile stained. There was an indefinite loss of weight. Examination on admission revealed no essential abnormalities, and the presumptive diagnosis was high intestinal obstruction, possibly on the basis of duodenal atresia.

Roentgen examination showed little gas in the bowel on the right side of the abdomen and apparent dilatation in the upper portion of the bowel on the left side. The mother stated that the infant sneezed constantly, with noisy breathing; the appearance of liquid stools during the first few days seemed to suggest the presence of infection. However, roentgenograms taken subsequent to a barium sulfate meal and a barium sulfate enema were diagnostic. The large bowel ended at the splenic flexure, and the barium meal showed distinct dilatation of the proximal portion of the duodenum. This suggested that there was an anomaly of rotation of the bowel with the concomitant presence of failure of fusion of the mesentery.

The diagnosis was confirmed by laparotomy. The cecum was found under the spleen, and there was considerable dilatation of the duodenum with rotation of the bowel about the superior mesenteric artery. A duodenojejunostomy was performed, and the child has made an uneventful recovery.

Ataxia in a Child with Hydrocephalus. EDWARD B. PLATTNER, M.D.

This child is a 21 month old white boy, admitted to the hospital in October with a history of walking unsteadily for nine months prior to admission and of tremor of the upper extremities for three months. He was born by spontaneous delivery at full term, weighed more than 8 pounds (3,630 Gm.) at birth and apparently developed normally; he sat at 5 months; teething was normal. He began to walk unassisted at 9 months of age, although the mother said he seemed to require some support, and at no time has he walked more than nine or ten steps. He fed himself at 10 months of age, but the mother noted that he spilled his food; there was noticeable tremor when he attempted to pass anything to the mouth.

The head is large and the fontanel open. He was irritable on admission but is pleasant now. The mother said he was able to talk but little. He has a somewhat steppage gait and tends to lean to the left. Study of the skull showed nothing abnormal except the open fontanel. Because of the high initial spinal fluid pressure and the tendency to fall to the left, a space-occupying lesion was suspected. Pneumoencephalography revealed pronounced internal hydrocephalus.

This is an unusual manifestation of pronounced hydrocephalus with symptoms suggesting intracranial pathologic changes, which are not confirmed.

Tetanus in an Infant. EDWARD B. PLATTNER, M.D.

This 2 month old Negro girl was brought in with a history of trismus for twenty-four hours prior to admission. She had been apparently well, was breast fed and seemed normal. The mother said she had noted difficulty in nursing, and it was necessary to pry the mouth open to insert the nipple. The past history and dietary history were adequate. The only significant conditions observed on physical examination were difficulty in opening the mouth and irritability.

On admission several diagnoses were considered: ankylosis of the temperomandibular joint, tetany and meningitis and a lesion of the central nervous system to account for the irritability. There was increase in irritability; the neck was rigid, and the fists were clenched. Roentgen

examination and determinations of blood chemistry showed nothing suggestive of tetany. The calcium and phosphates were in normal relationship. The spinal fluid was normal.

During the periods of irritability there was some frothing resembling tetanus. Because of the irritability she was treated with sedatives. Phenobarbital was given (0.5 Grain [0.03 Gm.] three times daily) without effect; seconal sodium caused the trismus to relax slightly. Ten thousand units of tetanus antitoxin followed by 20,000 units two days later was administered. Pentobarbital sodium was given by mouth whenever a spasm occurred. Fluids were given parenterally. Gradually the spasms were controlled, and in two weeks they disappeared completely. Recovery was spontaneous. There was never any sign of pulmonary involvement.

DISCUSSION

DR. JOSEPH K. CALVIN: I should like to ask whether there was any evidence of trauma. When there is no fever, the prognosis is better than when the temperature is elevated. The mortality seems to be in proportion to the complications rather than to tetanus per se.

DR. BERNARD GUMBINER: There was no roentgen evidence of compression fracture or other trauma.

DR. A. H. PARMELEE: Could this have been tetanus of the newborn? What is the incubation period for tetanus?

DR. E. D. PLATTNER: In the newborn, the incubation period is usually ten days to two weeks. This baby was delivered at Provident Hospital, and, so far as we could judge, the history was normal until twenty-four hours prior to her admission here.

DR. M. L. BLATT: Tetanus may result from a secondary injury when there has been a primary injury months before. The incubation period must be more than two weeks, for I know of cases in which it developed after a longer time.

My associates and I have a team of nurses and doctors to take care of tetanus in both children and adults. The results have been much better than those we obtained before the team was organized. The nurses may be on duty elsewhere, but as soon as a patient with tetanus is brought in the group is assembled and the patient is never left for a moment. We analyzed our cases some time ago. Only 2 or 3 patients had had injuries sufficiently significant to cause them to consult a physician, and these traumas were not considered severe enough to warrant administration of tetanus antitoxin. The others had had such insignificant injuries that a physician was not consulted until tetanus developed.

Scurvy. I. M. LEVIN, M.D.

These 2 patients were admitted to the hospital with infection of the upper respiratory tract. The 9 month old Negro boy was brought in because of a cold and anorexia extending over a period of several weeks. He had been fed a formula consisting of 12 ounces (360 cc.) of evaporated milk and 6 ounces (180 cc.) of water; cod liver oil and orange juice supposedly had been given.

The child was unable to sit up. The anterior fontanel was large and the head somewhat square. Umbilical hernia was present. The tongue seemed large, but other conditions observed on physical examination were insignificant. Studies of cholesterol showed normal values. Chemical examination of the blood disclosed: ascorbic acid 0.2 mg. per hundred cubic centimeters, calcium 9.20 mg. and phosphorus 2.56 mg., and phosphatase activity 5.16. He was given 100 mg. of ascorbic acid daily and calcium gluconate. Blood levels then were normal.

Two examinations of the blood showed a moderate degree of sickling. Roentgenograms disclosed three centers of ossification in the wrists, periosteal thickening of the long bones, dense epiphysial shadows and flaring of the long bones. The final diagnosis was sickle cell anemia, rickets and healing scurvy.

The second patient was 14 months old and had never been able to sit up. The mother was treated for syphilis after the birth of this child, her third illegitimate premature infant. When the infant was 7½ months of age the right humerus had been fractured, but it had healed. The child was admitted to the hospital with an infection of the upper respiratory tract and painful extremities.

There was a saddle nose with congenital absence of the anterior portion of the nasal septum. The ribs showed beading; the chest was pigeon shaped. There were no teeth. Ecchymoses were noted over the upper and lower areas of the arms and above the knees. Swelling of the left elbow and right leg was present. There was definite crepitus at the distal end of the left humerus with easy displacement of the distal portion.

On first consideration the infant appeared to have congenital syphilis with Parrot's pseudoparalysis, although his age was against this diagnosis. Results of chemical examination of the blood were within normal limits: nonprotein nitrogen, 33.0 mg. per hundred cubic centimeters; total ascorbic acid, 0.5 mg.; protein, 6.90 Gm.; albumin, 4.62 Gm.; globulin, 2.28 Gm.; calcium, 10.3 mg., and phosphorus, 6.63 mg.; the phosphatase activity was 21.53 units (Bodansky). Just an increase of the intake of orange juice for a couple of weeks raised the ascorbic acid level to 1.05 mg. per hundred cubic centimeters.

We have observed that the majority of infants under 6 months of age with congenital syphilis have low ascorbic acid levels. In such a case we administer 100 mg. daily. In spite of the fact that the level rises to normal, treatment by the intensive five day method, developed in this institution, is almost invariably followed by a fall in the level, though ascorbic acid is given at the same time. I feel that infants should be given ascorbic acid at an earlier age and in larger dosage than in the past. Inability to absorb or some error in the metabolism of ascorbic acid unquestionably results in unrecognized subscorbutic states. Some of the osseous changes ascribed to congenital syphilis by earlier observers are in all likelihood evidence of subrachitic and subscorbutic disturbances.

The Kahn and Wassermann reactions of this infant were all negative after repeated checking. The mother's serologic reactions were negative. Two previous children were stillborn. We see many instances of a negative Kahn reaction in the mother and a positive reaction in the child; also negative Kahn and positive Kollmer reactions are encountered.

Roentgen studies revealed classic extensive periosteal changes in the left humerus with a large amount of subperiosteal calcification. There were similar changes but of lesser degree in the lower portion of the radius. There was a narrow transverse line of absence of bone density at the ends of the radiuses and ulnas. The lower extremities revealed periosteal elevation and widening and irregularity in the lower ends of the femur and tibia, but to a lesser degree than in the upper extremities.

The conditions observed were those of periosteal hemorrhage due to scurvy with associated rickets.

Infants receiving intensive five day venoclysis of mapharsen for congenital syphilis will take full feedings in addition to the 300 cc. of 5 per cent solution of dextrose.

Ascorbic acid levels as ordinarily determined in most institutions are open to question. Exclusive of the error resulting because of the time elapsing between time of withdrawal of blood and determinations, it is doubtful whether the plasma levels truly indicate the presence of scurvy. The level of ascorbic acid of the cells themselves is apparently the truest index.

The following cases were also presented:

Chronic Nephritis with Intractable Hypertension. PHILIP L. ARIES, M.D.

Rickets and Chronic Nephritis. CRAIG D. BUTLER, M.D.

Book Reviews

The Biological Action of the Vitamins. Edited by E. A. Evans Jr., Associate Professor of Biochemistry, The University of Chicago. Price, $3.00. Pp. 227, with 33 illustrations and 10 tables. Chicago: The University of Chicago Press, 1942.

This volume is a collection of papers presented as a symposium sponsored by the University of Chicago and the University of Wisconsin in connection with the celebration of the fiftieth anniversary of the University of Chicago. They were presented at Chicago, Sept. 15 to 19, 1941. A companion volume, "Respiratory Enzymes," consisting of papers presented at Madison, Wis., has been published by the University of Wisconsin Press.

The list of titles and authors is as follows: "The Biological Action of the Vitamins," by C. A. Elvehjem, Ph.D.; "Cocarboxylase," by S. Ochoa, Ph.D.; "Vitamin B_1: Clinical Aspects," by Norman Jolliffe, M.D.; "Riboflavin," by Paul György, M.D.; "Human Riboflavin Deficiency (Ariboflavinosis)," by W. H. Sebrell, M.D.; "The Story of Pellagra and Its Treatment with Nicotinic Acid," by David T. Smith, M.D.; "Pyridoxine," by S. Lepkovsky, Ph.D.; "Pantothenic Acid and the Microbiological Approach to the Study of Vitamins," by Roger J. Williams, Ph.D., D.Sc.; "Pantothenic Acid in Human Nutrition," by Edgar S. Gordon, M.D.; "Biotin," by Vincent du Vigneaud, Ph.D.; "Choline," by Wendell H. Griffith, Ph.D.; "The Economy of Phosphorus in the Animal Organism," by Franklin C. McLean, Ph.D., M.D.; "Vitamin K," by D. W. MacCorquodale, Ph.D.; "Vitamin K: Clinical Aspects," by H. P. Smith, M.D., and E. D. Warner, M.D.

The first essay, by Professor Elvehjem, outlines two major stages in the development of knowledge of the biologic activity of vitamins: first, before the relation between vitamins and respiratory enzymes was recognized; and, second, since this development. During the first stage histologic studies of tissues from vitamin-deficient animals led to recognition of such fundamental phenomena as the metaplasia of epithelium characteristic of vitamin A deficiency and the lack of formation of intercellular substance in vitamin C deficiency. The second stage was inaugurated when "the scientific efforts in this field [the chemistry of the vitamins] and those in the field of respiratory enzymes collided. We are still busy following the sparks from this impact."

The remaining papers are by distinguished investigators who have made important contributions in the fields which they discuss. The majority concern laboratory studies, but clinical applications are not neglected, and indeed, three of the fourteen papers are primarily concerned with clinical aspects. The majority of the essays are concerned with vitamins of the B group, but there are in addition papers on biotin, choline and vitamin K. One of particular interest to the reviewer is entitled "The Economy of Phosphorus in the Animal Organism." It outlines in bold strokes a comprehensive picture of phosphorus metabolism, of which the process of calcification and the function of vitamin D are only parts. Like many of the other papers it is valuable not only for the report of new facts but for its stimulating ideas and theories.

The book is attractively printed and bound. A bibliography follows each paper. There is, however, no index.

Familial Nonreaginic Food-Allergy. By Arthur F. Coca, M.D. Price, $3.00. Pp. 160, with 20 tables and 12 charts. Springfield, Ill.: Charles C Thomas, Publisher, 1943.

Dr. Coca's short monograph on a new adventure in the field of allergy is provocative and will be read avidly by all interested in allergy. Unfortunately, it will have little value for pediatricians, even though the alluring title, "Familial Nonreaginic Food-Allergy," may tempt them, for they are generally intrigued by texts dealing with food.

The main thesis of this volume is that certain persons who are sensitive to food and do not present positive cutaneous reactions regularly have an acceleration of pulse rate during their allergic episode. On this thesis is based "a new method of approach" to the diagnosis and treatment of a group of allergic diseases. One may wonder at the assumption that dementia praecox is due to food allergy. "All subjects of dementia praecox thus far studied," states Dr. Coca, "have exhibited the typically food-allergic pulse." He also contends that a study of epileptics "by the method of the pulse controlled trial-diet has provided preliminary evidence of the food-allergic nature of idiopathic epilepsy."

Allergy has traveled on many tortuous paths, and this seems a strange one indeed. Perhaps the pulse rate does increase during allergic episodes, as it does in many physiologic disturbances. Surely this symptom is an extremely fickle one, and it seems difficult to conceive that it can be regarded as of special significance in the evaluation of so chronic and insidious a condition as allergy. Furthermore, the short range of increase in pulse rate that Dr. Coca regards as pathognomonic would not be impressive to those interested in children, who think nothing of a bounding pulse with 120 or more beats a minute resulting from countless causes.

The reviewer doubts that Dr. Coca's theory will arouse more than passing interest. On the other hand, in all fairness to the author, it must be stated that this volume is merely a preliminary report and further reports should be awaited before final judgment is passed.

Fundamentals of Immunology. By William C. Boyd, Ph.D. Price, $5.50. Pp. 446, with 45 illustrations and 67 tables. New York: Interscience Publishers, Inc., 1943.

In the preface, the author states that his purpose is to introduce immunology to "medical students, chemists, biologists and others interested in an understanding of the basic principles of the science." He points out that his book may be of service to persons who wish to undertake research on the subject.

Clearly, the book is not for clinicians if their interest in it is solely in the practical applications of immunology, for the material on this phase of the subject is incomplete, occasionally outdated and rarely inaccurate.

The chemistry of antigens and antibodies is exhaustively treated. Although the author states that his subject matter is for beginners, it is doubtful that the bulk of the data presented will be understandable to persons not thoroughly grounded in both inorganic and organic chemistry. Many classic concepts in immunology are "debunked" and explained in chemical terms. But to state that the subject is thereby clarified for the beginner would be far from the truth.

However, the book will doubtless have a far reaching effect in eventually producing order in a field now full of confusion. To the researcher in immunology, it should be of immense value for its attempt to explore every portion of the field and for the extensive bibliography.

Glimpses Into Child Life. By Rose Zeligs, Ed.D. Price, $3.00. Pp. 440, with 2 tables. New York: William Morrow & Co., 1942.

This book summarizes the observations of a well trained progressive educator of 12 year old children. After many years of experience in teaching the sixth grade and from careful study of individual children, the author records her impressions of children of this age. Much of the data is derived from questionnaires given to her classes, and the greater number of her conclusions are based on open class discussions. These tests and discussions give an accurate picture of the attitudes, ideas and feelings of children of this age—or of as many of the ideas and feelings as children of this age are willing to express in open forum.

In addition to the objective observations on children, the author expresses herself freely on parents, discipline and methods of rearing children. Here it must be remembered that she is a teacher of a sixth grade and is expressing herself as one who looks back on children and forward to their adulthood from this point in terms of this age group. Since growth and development are not discussed, one would question some of her conclusions.

Chapters on social thinking, health instruction and sex instruction are good. The most valuable chapters in the book deal with creative writing. Here one sees a good school teacher at her best, again demonstrating that there is much in the minds of children which will come out in free expression if given a chance.

Therapeutics of Infancy and Childhood. Edited by Drs. Harry R. Litchfield and Leon H. Dembo. Price, $32. Four volumes and desk index volume. Over 600 illustrations, with 38 plates in full colors. Philadelphia: F. A. Davis Company, 1942.

This four volume (plus one index volume) system of therapeutics of infancy and childhood is a beautifully printed and illustrated treatise. Many of the colored illustrations are remarkably good and evidently are from photographs.

The names of many of the contributors are not as impressive as one might desire for an authoritative treatise of this magnitude. The whole field of therapy is covered in the 4,000 pages of text, even such adjuvants as drug legislation and patent medicine. There is an extensive chapter on sulfonamide drugs, and detailed instructions are given for paracentesis of various body cavities and for administration of oxygen. Parenteral administration of fluids, physical therapy and fever therapy are among other subjects covered. Radio therapy is likewise given detailed consideration, and there are chapters on therapy with respect to

various diseases and systems of the body. The conception of the book is broad, and the whole treatise should afford much valuable information of sufficiently detailed character to be of practical use.

The Sight Saver. By C. J. Gerling. Price, $2.00. Pp. 202, with 1 illustration. New York: Harvest House, 1943.

This is a book written for laymen and is intended as a practical reference for those who desire a concise and understandable answer to the many questions which arise concerning the eye. It could also be used as a simple "refresher" for the physician who seeks to explain the visual mechanism to his patients. Its form is that of an encyclopedia, with the subject matter arranged alphabetically. While this arrangement sacrifices a certain amount of readability, it makes reference to separate topics much easier. The book departs from the usual one of this type in that much space is given not only to the normal anatomy and physiology of the eye but to the exposure of quack remedies, fake eye washes and illegitimate use of "exercises" for near sightedness and diseases of the eye. There is also an interesting discussion of glasses and how they should be chosen. At this time, when the visual requirements for the armed forces have focused the public's attention upon the eye and when so many physicians are besieged by questions on the preservation of vision, this book should be a real help. It might also be recommended as a reference book for social workers, nurses, nurses' aides and medical office assistants.

So You Feel Sluggish Today. By Harry A. Gauss, M.D., Assistant Professor of Medicine, University of Colorado School of Medicine, Denver. Price, $3.00. Pp. 291, with 37 illustrations. Boston: The Christopher Publishing House, 1942.

This book is a treatise on constipation written by a physician for the layman. It is well organized and not too technical and contains a liberal number of cartoons, drawings and charts.

After a short anatomic description of the digestive tract the author discusses the relationship of habits, foods, fatigue, allergy and drugs to constipation. A discussion of the atonic colon, the spastic colon, the redundant colon and mucous colitis comprises the midportion of the book. Dietary advice, lists of various foods and vitamins, a set of exercises and a glossary of medical terms complete the volume. Throughout the book there is a liberal sprinkling of references to the published articles of various other gastroenterologists.

This book should help to prevent the patient with constipation from indulging in some of the bizarre practices which are all too prevalent.

The Metabolic Cost of Maintaining a Standing Position; with Special Reference to Body Alignment. By Harriet Graham McCormick. Price, $1.25. Pp. 75, with 9 illustrations. New York: King's Crown Press, 1942.

This monograph presents in detail a study performed with healthy young women as subjects, designed to determine the degree in which gaseous metabolism is increased in the erect versus the recumbent position during the postabsorptive state. The posture of each subject was analyzed, and the relative metabolic cost for different standing positions was compared statistically. The data indicate that less energy is required when support is based on ligamentous bracing of joints than when the position is maintained through muscular balance. In other words, the position assumed with fatigue is more economical physiologically than is the posture of readiness for response, usually accepted as the desirable standing position. The difference of expenditure of energy between these two postures, though statistically significant, is not appreciable when compared with the cost of other factors which continuously are in operation in an active subject.

Infección y sulfonamidoterapie en trastornos digestivo-nutritivos y enteritis del lactante. By Victor Zerbino. Price, none given. Pp. 137, with 11 graphs. Montevideo, Uruguay: García Morales, 1942.

The author states that in Uruguay 60 to 80 per cent of the cases of acute nutritional disturbances are due to parenteral infection. Fifty per cent of these are due to Salmonella or Shigella organisms and the remainder to various other organisms. A sulfonamide compound was used in the treatment of 384 children, with a resulting mortality of 1.2 per cent. Sulfathiazole, sulfadiazine or sulfaguanadine were the most effective against all infections except those due to Salmonella, for which he believes succinylsulfathiazole to be better suited. This treatment has reduced the general mortality of children from between 38 and 45 per cent to between 18 and 12 per cent.

The book is well written and contains an excellent bibliography and graphs.

Better Homes and Gardens' Baby Book. By Gladys Denny Shultz. Price, $2.50. Pp. 258, with numerous illustrations. Des Moines, Ia.: Meredith Publishing Company, 1943.

This book, written by a lay person but one who had the wisdom to consult an excellent pediatrician, should be of much use to any young mother with her first or later baby. It contains minute instructions on many useful matters, and if the advice is heeded it should in most instances remove a great deal of fear of consequences from such trivial things as thumb sucking. The book is well written and is attractively printed and illustrated. It has many useful items in it not to be found in the ordinary book, such as recipes for making special dishes, outlines of diets for a long period, vitamin content of foods and at the end of the book a record section, which is most complete. It is a book which should be most useful to the laity and might be read with profit by physicians.

Deshidratación en pediatría. By Drs. Mario J. del Carril and Alfredo E. Larguia. Price, not given. Pp. 370, with 18 illustrations, 53 tables and 33 graphs. Buenos Aires: El Ateneo, 1943.

This book, in Spanish, is an interesting discussion both from the physiologic and from the clinical standpoint on the subject of water and mineral balance in children. Early chapters deal with the normal balance and are followed by a discussion of pathologic conditions in which dehydration results. The text is fully explained by numerous tables and graphic illustrations. An appendix has been added, which contains the indications and procedures for use of plasma in these conditions. The bibliography is excellent and well chosen.

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